10-1-1969

Volume 12, issue 4

Canadian Medical Association

HISTORY OF CANADIAN SURGERY

SURGICAL HISTORY OF PULMONARY TUBERCULOSIS: THE RISE AND FALL OF VARIOUS TECHNICAL PROCEDURES*

GODFREY L. GALE, M.B., Ch.B., F.R.C.S.(Edin.) and
NORMAN C. DELARUE, M.D., M.S.(Tor.), F.R.C.S.[C], F.C.C.P., F.A.C.S.,
Toronto, Ont.

In 1904 the Toronto Hospital for Tuberculosis was opened on a 49-acre tract of farmland near the little country town of Weston, Ontario. In the next 26 years 7181 adult patients were treated at the Hospital: of these 3221 died from tuberculosis—a case mortality rate of 44.9%. The Hospital's annual report in 1930 also stated with some satisfaction that, over this same period, 31.1% of the patients had been discharged as "improved", but admitted with commendable honesty that only five (0.07%) had been discharged in an "apparently arrested" condition! In this same year Drs. J. C. McClelland and R. I. Harris organized a surgical service in the Hospital. Dr. R. M. Janes joined this service in 1932.

This paper describes the rise and fall of nine surgical procedures in this hospital over the 38-year period, 1930 to 1967. For present purposes, artificial pneumothorax and artificial pneumoperitoneum are classed as "surgical" procedures, in contrast to bed rest and graduated exercise, good food, heliotherapy and ultraviolet light, gold injections and tuberculin injections, which were the only other definitive treatments available until antibiotics came into use in 1947.

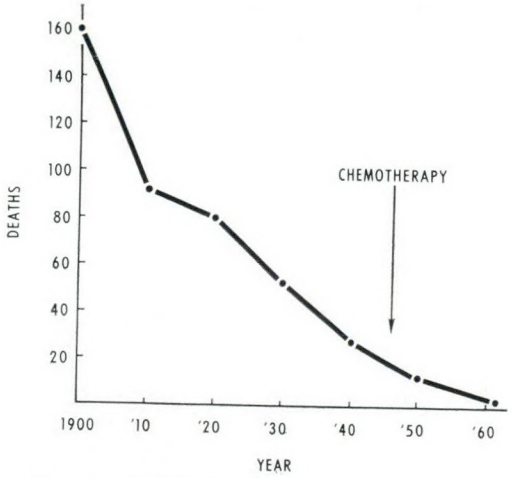

Fig. 1.—Annual deaths from tuberculosis in Ontario per 100,000 population, from 1900 to 1960 (after Blaisdell).

It should be pointed out that, in the western world, tuberculosis mortality per 100,000 population started to decline more than 100 years ago, primarily because diet and living standards had improved, infectious cases were segregated, general knowledge of hygiene had increased, but perhaps also because the genetic resistance of the host was gradually increasing. The number of deaths from tuberculosis in Ontario has declined progressively since 1900 (Fig. 1). The *case mortality rate* of all forms of tuberculosis, however, remained high until antibiotic therapy became available.

Surgical Procedures

Artificial Pneumothorax

This temporary and reversible collapse of the lung was originally proposed by Forlanini[1] in 1882 to reduce the high mortality associated with tuberculous cavities. In 1898 J. M. Rogers of Ingersoll, Ontario did the first artificial pneumothorax in Canada. This procedure was introduced into the Toronto Hospital for Tuberculosis during the First World War and, in the early years, was attempted in about 5% of admissions. As the staff gained confidence, it came into wider use and, at the height of its popularity in the 1930's, was attempted in 60% of all admissions, and a pneumothorax was established in 75% of those in whom it was attempted (Fig. 2). At the Toronto Hospital, bilateral pneumothorax was induced in one-fifth of all patients with bilateral disease. A peak was reached in 1939 when artificial pneumothorax was successfully induced in 152 new cases

*From the Toronto Hospital for Tuberculosis, Weston 492, Ont.

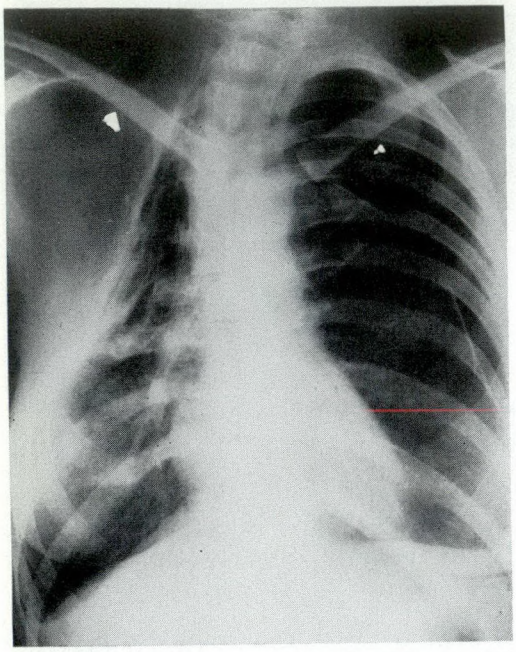

Fig. 2.—C.E. Chest radiograph February 27, 1948. On the left a successful pneumothorax has been established, on the right a standard, seven-rib thoracoplasty.

(Fig. 3). In 1943, 11,999 individuals had an established pneumothorax "refilled" as inpatients or outpatients. When the patient had a cavity that was held open by string adhesions the surgeon attempted to sever these by thoracoscopy and intrapleural pneumonolysis. Occasionally open pneumonolysis was performed.

Although artificial pneumothorax undoubtedly closed cavities and converted

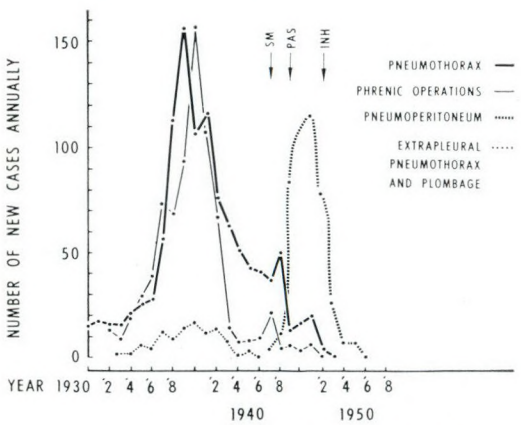

Fig. 3.—The rise and fall of pneumothorax, phrenic nerve operations, extrapleural pneumothorax and pneumoperitoneum at the Toronto Hospital for Tuberculosis.

sputum in many patients who might otherwise have died, its use was not without danger. Pyogenic or tuberculous empyema were grave complications. Even if infection did not develop, a fibrin "peel" occasionally formed over the visceral pleura and often prevented re-expansion of the lung. As the case mortality rate declined, the procedure was gradually dropped from the therapy of pulmonary tuberculosis.[2] No patient with "new" tuberculosis has been treated by pneumothorax in this hospital since 1952. However, a few patients with inexpandable lungs still attend the outpatient clinic for periodic air refills; these are patients who are unsuitable for decortication or unwilling to undergo that procedure. In the years 1930 to 1952 a pneumothorax was successfully induced in 1067 patients.

Operations on the Phrenic Nerve

Because cavitary disease in the lower lobes was often poorly controlled by pneumothorax, operations on the phrenic nerve were introduced to paralyze the diaphragm temporarily or permanently. These procedures were used either in conjunction with a pneumothorax or as the primary, definitive treatment. Under local anesthesia, the phrenic nerve was approached above the clavicle and, if temporary paralysis was required, the nerve was crushed once. The diaphragm usually recovered in four to six months although, in spite of the greatest care, the paralysis was sometimes permanent. If the surgeon intended to produce permanent paralysis he divided the nerve and, in some cases, avulsed the distal segment to disrupt the accessory phrenic nerve if it was present (Fig. 4).

Phrenic nerve operations were first performed at the Toronto Hospital for Tuberculosis in 1932. During the 38-year period covered in this paper 732 patients underwent this operation, reaching a peak in 1940 when it was done in 153 patients (Fig. 3). Its rise in popularity and subsequent decline paralleled closely those of artificial pneumothorax. In this hospital, no definitive phrenic nerve operation has been done since 1951. However, temporary phrenic paralysis is occasionally used today

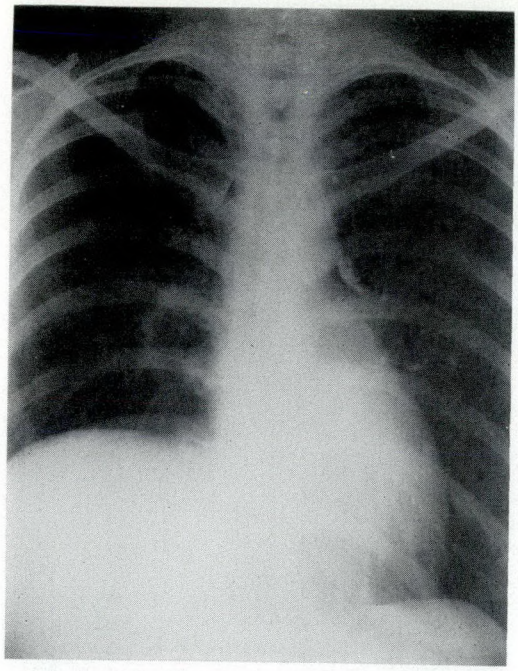

Fig. 4.—A.O. Chest radiograph August 19, 1940. The right phrenic nerve has been crushed. The disease in the right lung has cleared well.

to obliterate the pleural space after a lobectomy or a segmental resection.

Scalenotomy

This procedure was done in four patients in 1932 and in one patient in 1939. The scalene muscles were divided close to their insertions at the first and second ribs to relax the apex of the lung. By this means the surgeon hoped to promote the closure of apical cavities. The procedure was not successful and was soon abandoned.

Extrapleural Pneumothorax and Plombage

This procedure was used in those patients who had an apical cavity that did not collapse after a pneumothorax, usually because of extensive adhesions which could not be divided by pneumonolysis. The surgeon resected a small portion of an upper, posterior rib and developed a plane outside the parietal pleura, between it and the endothoracic fascia. Thus, without opening the pleura, the whole apex of the lung was freed and pushed down. The resulting space under the upper ribs

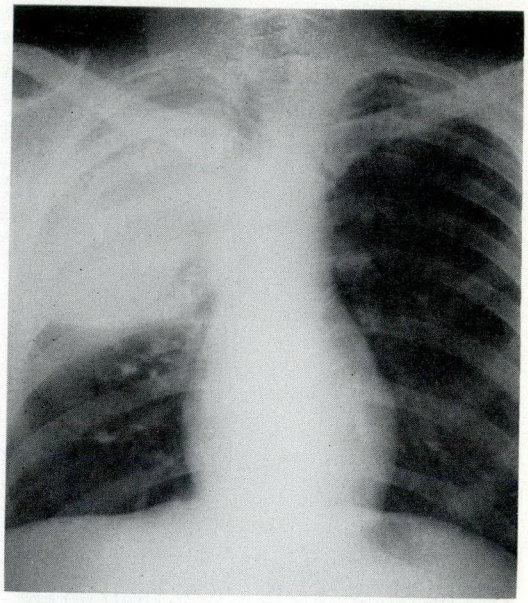

Fig. 5.—E.W. Chest radiograph September 23, 1950. An extrapleural collapse is maintained by Gomenol oil.

was maintained by regular refills of air, by Gomenol oil (a substance believed to have a bacteriostatic effect on tubercle bacilli), by paraffin oil or paraffin wax (Fig. 5).

This operation, first performed in this hospital in 1933, was never widely used. In all, 98 patients were so treated. It reached a peak in 1940 when 15 patients underwent this operation (Fig. 3). The procedure had serious drawbacks. The collapse, once established, was irreversible. Any infection that developed in the space, whether tuberculous or pyogenic, was difficult to treat: one such patient died when hemorrhage into the space proved impossible to control. In one patient, in whom the space had been filled with paraffin (paraffin plombage), a paraffinoma developed around the esophagus producing obstruction that was only relieved by a colon bypass. After a few years, this procedure was abandoned and has not been used since 1945.

Pneumoperitoneum

Therapeutic pneumoperitoneum was originally proposed as a method for treating tuberculous peritonitis. With the decline of artificial pneumothorax, this pro-

cedure was used for a few years to treat patients with bilateral pulmonary disease or with basal cavities which, because of their position, could not be collapsed by thoracoplasty. The procedure, which was relatively safe and completely reversible, was first used in this hospital in 1947 (Fig. 6). Pneumoperitoneum reached its peak in 1951 when it was done on 112 new patients and 9167 refills were given (Fig. 3). In all, 431 patients received this treatment. It was, however, of limited value and once chemotherapy was introduced it ceased to play any part in the treatment

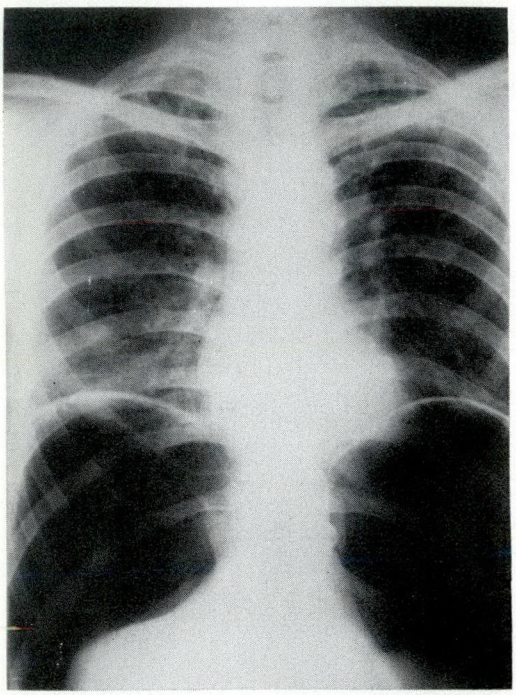

Fig. 6.—R. W. Chest radiograph June 10, 1953. A pneumoperitoneum has been established. Parenchymal disease has cleared well.

of pulmonary tuberculosis. No new case has been treated in this way since 1955. Today, in the postoperative management of pulmonary resections and decortications, pneumoperitoneum is occasionally used to elevate the diaphragm and obliterate a residual air space.

Monaldi Drainage

In 1938 Monaldi introduced his technique of inserting a catheter through the chest wall into large cavities.[3] Suction was

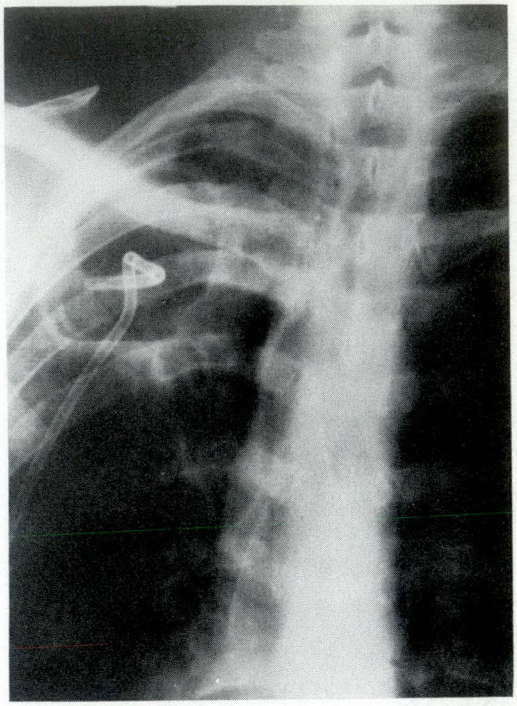

Fig. 7.—J.B. Chest radiograph October 22, 1941. Monaldi drainage. An indwelling catheter drains a large cavity at the right apex. This cavity later closed.

then applied to reduce the size of the cavity so that it would heal or collapse after thoracoplasty. At the Toronto Hospital for Tuberculosis two of these operations were done in 1940, six in 1941 and two in 1946, a total of 10 cases. This operation proved, however, to have little value and it has not been performed since 1946 (Fig. 7).

Thoracoplasty

Before the First World War, surgeons suggested that sections of ribs be removed to collapse a portion of the lung permanently. The concept of selected and graded thoracoplasties was developed in North America by Alexander.[4] The first thoracoplasty at this hospital was performed by R. M. Janes in 1933 and subsequently 1011 patients were so treated. The procedure reached its peak in 1949 when 98 patients underwent 179 "stages" of this procedure (Fig. 8). In the past 25 years, a period during which 1265 operative stages were done in 699 patients, 11 have died during

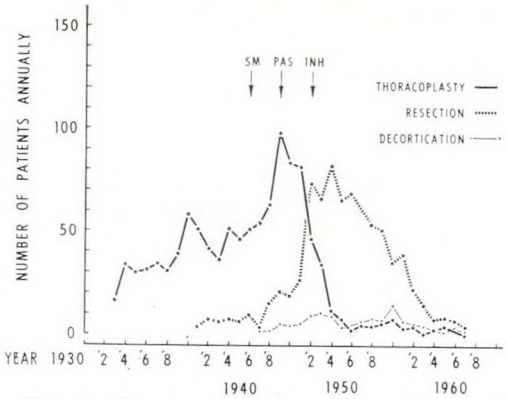

Fig. 8.—The rise and fall in thoracoplasty, pulmonary resection and decortication at the Toronto Hospital for Tuberculosis.

or immediately after operation—a rate of 1.6%; the procedure is relatively safe even in the elderly.[5]

The "standard" thoracoplasty was done in one to four stages depending on the number of ribs removed and whether or not the anterior ends of the ribs were also removed. The surgeon excised the corresponding transverse processes except for the first thoracic transverse process which was preserved to protect the first thoracic nerve root (Fig. 2). Occasionally part of the scapula was removed if the inferior angle impinged on the remaining ribs. The Schede thoracoplasty removed all the structures of the chest wall in the operative area except for the skin and subcutaneous tissue.

In a few patients with tuberculous empyema, the surgeons at the Toronto Hospital for Tuberculosis did a thoracoplasty and the Eloesser procedure—a skin flap was turned in to create a permanent epithelialized track for drainage. The Semb thoracoplasty consisted of an "apicolysis" and removal of the upper ribs. The operator developed a plane between the parietal pleura and the endothoracic fascia and stripped the apex downwards extrapleurally. An apical cavity was thus compressed from above down as well as from side-to-side (Fig. 9). The Björk thoracoplasty was an osteoplasty in which varying lengths of the posterior ends of the ribs were removed. The remaining portions of the ribs were then twisted down at their costal cartilages and wired in place to form a new, rigid, horizontal roof for the chest at the required level.

Once antibiotics had been introduced pulmonary resection became safe and the popularity of thoracoplasty rapidly declined. Resection was clearly a better procedure if dangerous residual disease could be removed rather than compressed under a thoracoplasty. The last thoracoplasties undertaken at the Toronto Hospital for Tuberculosis as definitive procedures were done in 1960. At present the

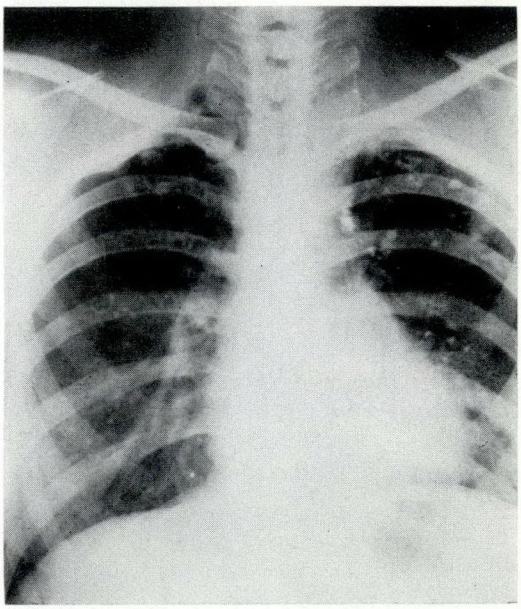

Fig. 9.—E.K. Chest radiograph January 18, 1957. Bilateral, four-rib, Semb thoracoplasty with apicolysis, done in 1949, closed the apical cavities.

only indications for a thoracoplasty are: (1) empyema in which decortication is not feasible; (2) bronchopleural fistula with a residual air space following resection, and (3) post-pneumonectomy infection within the hemithorax.

Cases fulfilling these indications are rare (Fig. 8). When it is necessary, we use the procedure introduced by F. G. Kergin—thoracoplasty with parietal pleurectomy. The requisite rib lengths are removed subperiosteally carefully preserving the intercostal muscles and their neurovascular bundles. The operator then removes the thickened, rigid, parietal pleura, and the living muscle bundles are allowed to fall on the underlying lung or mediastinum.

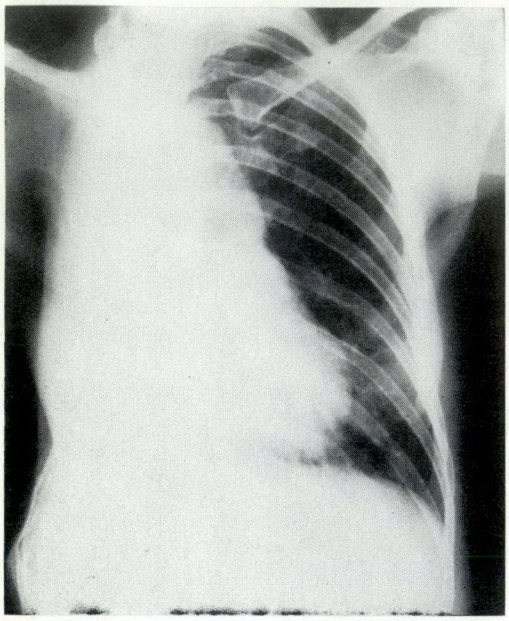

Fig. 10.—L.B. Chest radiograph November 17, 1961. A post-pneumonectomy empyema was cured by a right, ten-rib thoracoplasty and parietal pleurectomy. The patient is now in good health.

The ribs then regenerate in their permanently collapsed position (Fig. 10).

Pulmonary Resection

In 1941 R. M. Janes performed the first pulmonary resection for tuberculosis in this hospital—a pneumonectomy. This patient is still alive and well. Since 1941, 774 resections have been done for tuberculosis; many of these were true "salvage" operations.[6] The procedure reached a peak in the year 1954 when 83 resections were done on 80 patients; in three patients, the resection was bilateral. As antibiotics became available the number of resections rose and the number of thoracoplasties declined (Fig. 8). Table I compares the operative mortality to the antituberculous therapy available at the time.

Since 1954 the number of resections has declined because antituberculous therapy is more effective. Additional drugs were discovered which could be used if the tubercle bacilli became resistant to the three primary drugs: streptomycin (SM), para-aminosalicylic acid (PAS) and isoniazid (INH). If they take several drugs in full dosage for two years, few patients will not achieve permanent control of their disease. Very few patients with pulmonary tuberculosis now being treated for the first time require resection. Similarly, children who develop segmental or lobar atelectasis after primary infection no longer need resection.

At present the indications for resection are: (1) relapse of disease following previous antibiotic therapy (tubercle bacilli resistant to the primary drugs), especially if there is persistent cavitation. In patients residing in a harsh environment (e.g. Eskimos) or in chronic alcoholics, when

TABLE I.—Resection for Pulmonary Tuberculosis. Mortality Related to Type of Antibiotic Therapy

Treatment period	*Number of resections*	*Number of post-operative deaths*	*Mortality rate (%)*
Antituberculous therapy not available 1941 - 1946	45	7	15.6
"Inadequate" antibiotic therapy 1947 - 1952	177	4	2.3
"Adequate" antibiotic therapy 1953 - 1967	552	8	1.5

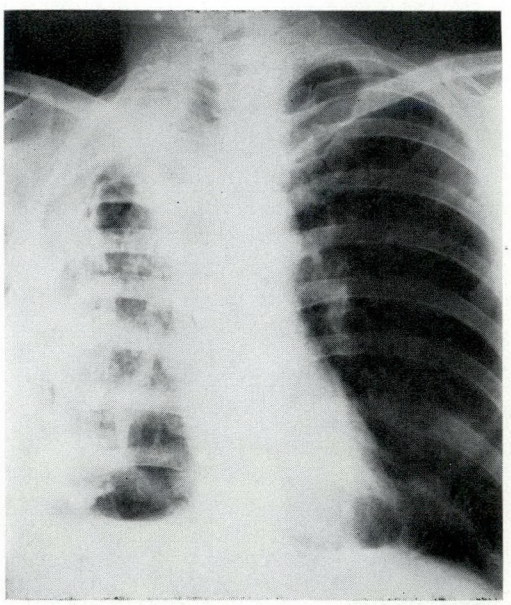

Fig. 11.—G.B. Chest radiograph January 8, 1968. The right lung has been largely destroyed by tuberculosis. There is a calcified empyema and a bronchopleural fistula.

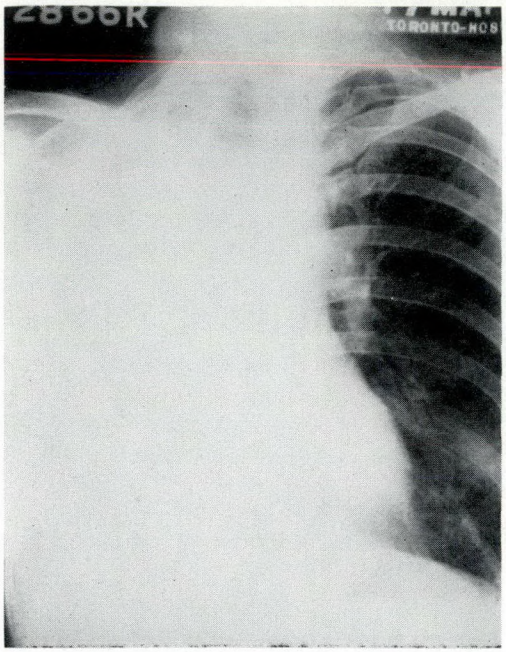

Fig. 12.—G.B. Chest radiograph May 17, 1968 showing a right pleuropneumonectomy.

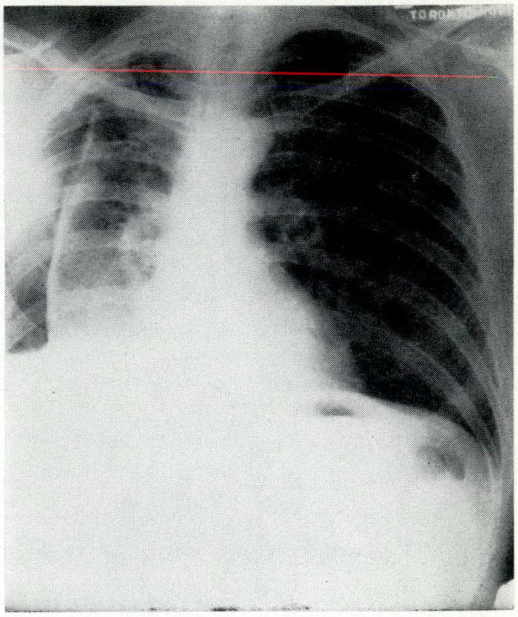

Fig. 13.—J.W. Chest radiograph May 24, 1966. After 29 years of pneumothorax, the right lung is inexpandable.

the physician cannot ensure that the patient will adhere faithfully to the required antibiotic program, there may be additional indications; (2) severe, post-tuberculous, lower-lobe bronchiectasis; and (3) a destroyed lung in a young person, especially when the lesion is associated with a tuberculous empyema and bronchopleural fistula (Figs. 11 and 12).

Decortication

The first decortication in this hospital was performed by F. G. Kergin in 1947. The patient, a teenage girl who was developing a fibrothorax following a tuberculous pleural effusion, achieved an excellent result. Of all the surgical procedures discussed in this paper, decortication is the only one in which the indications have not changed appreciably over the years. Furthermore, the frequency with which this procedure has been done has not varied significantly over the years although there was a peak in 1960 when 14 decortications were performed (Fig. 8).[7] The current indications for decortication are: (1) fibrothorax following certain cases of tuberculous pleural effusion; (2) tuberculous empyema; and (3) inexpandable lung following artificial pneumothorax (Figs. 13 and 14). At this hospital decortication was performed in 108 patients; only one died during or soon after operation.

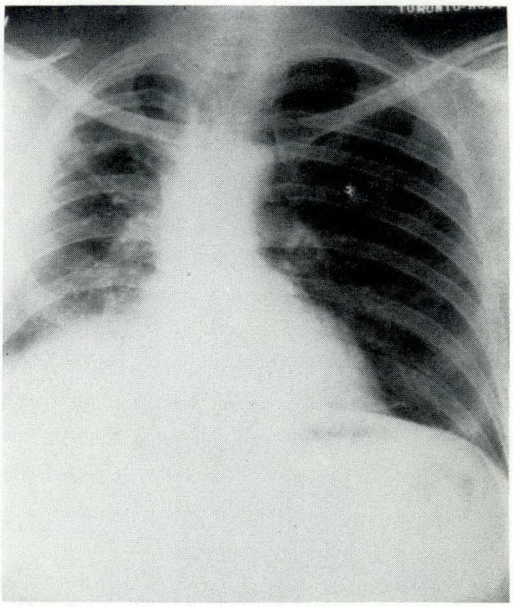

Fig. 14.—J.W. Chest radiograph July 21, 1967. The pleural space has been obliterated by a right parietal and visceral decortication.

Discussion

The effectiveness of any treatment for pulmonary tuberculosis must be determined by its influence on the case mortality rate, which declined little during the first three decades of this century. In the period covered in this report (1930 to 1967), nine surgical procedures were used at the Toronto Hospital for Tuberculosis most of which seemed to be useful at the time they were employed.

Today, however, antibiotic therapy is so effective that operative intervention is rarely needed. The first three drugs introduced—streptomycin, para-aminosalicylic acid and isoniazid are still the best drugs for initial treatment. In addition, six other "secondary" drugs are already in use: pyrazinamide, ethionamide, cycloserine, kanamycin, viomycin and isoxyl, and two more will probably be introduced shortly, namely ethambutol and capreomycin. Three other promising drugs, Rifampin (rifomycin-amino-methyl-piperazine), Thiacetazone (p-acetylaminobenzaldehyde thiosemicarbazone) and protheonamide are presently undergoing international clinical trial. If all of these agents prove effective, the physician will have 14 different drugs at his disposal when he treats tuberculosis. Because the present mortality rate from tuberculosis is very low and because no operative procedure is without risk, the indications for operation in pulmonary tuberculosis will probably be even more strictly limited in the future. However, a few patients will still require a thoracoplasty, resection or decortication.

Summary

This paper discusses briefly the rise and fall of nine different surgical procedures used in the treatment of pulmonary tuberculosis at the Toronto Hospital for Tuberculosis since 1930.

Most procedures played a useful part at a particular period in reducing the case mortality rate and the morbidity associated with pulmonary tuberculosis. However, in view of the many excellent drugs now available, the future indications for surgical treatment will probably be limited still further. Despite this, the occasional patient will still benefit from thoracoplasty, resection or decortication.

We wish to acknowledge with gratitude the help received from Drs. C. A. Wicks, H. E. Pugsley, H. S. Coulthard and D. R. Garrett. We also wish to pay a tribute to the late Dr. R. M. Janes and to Dr. F. G. Kergin for their pioneer work in the surgical treatment of pulmonary tuberculosis.

References

1. Heaton, T. G.: Artificial pneumothorax in pulmonary tuberculosis, 2nd ed., The Macmillan Company of Canada Ltd., Toronto, 1947, p. 15.
2. Phair, W. B.: The decline of artificial pneumothorax, *Canad. Med. Ass. J.*, **65:** 542, 1951.
3. Simmons, G.: Intracavitary aspiration, *Amer. Rev. Tuberc.*, **53** (Suppl.): 11, 1946 (abstract).
4. Alexander, J.: The collapse therapy of pulmonary tuberculosis, Charles C Thomas, Publisher, Springfield, Ill., 1937.
5. Beaconsfield, P., Coulthard, H. S. and Kergin, F. G.: Treatment of pulmonary tuberculosis by thoracoplasty in patients over 50 years of age, *Thorax*, **9:** 211, 1954.
6. Gale, G. L. and Delarue, N. C.: Salvage resections in patients with advanced pulmonary tuberculosis, *Canad. J. Surg.*, **8:** 267, 1965.
7. Gale, G. L. and Delarue, N. C.: Decortication in pleural and pulmonary tuberculosis, *Canad. J. Surg.*, **5:** 172, 1962.

ORIGINAL ARTICLES

AFFERENT LOOP SYNDROME*

J. ALEXANDER McINTYRE, M.D., F.R.C.S.[C], F.A.C.S. and
PAY-ZEN CHENG, M.B., *Toronto, Ont.*

AFFERENT loop syndrome, an uncommon complication of gastroenterostomy either alone or combined with a Billroth II gastrectomy, consists of a partial or complete closed-loop obstruction of the afferent jejunal loop with or without strangulation. Recently several articles dealing with the subject have appeared in the literature.[1-4] In view of the high mortality and morbidity associated with this syndrome, clinicians should keep it in mind when caring for a patient who has previously undergone gastric surgery.

Chronic afferent loop obstruction presents with recurrent episodes usually over a prolonged period. The acute syndrome manifests itself either immediately after operation or its onset may be delayed for many years.

Five patients with afferent loop obstruction have been encountered at St. Joseph's Hospital, Toronto, during the past six years. They are the subject of this report.

CLINICAL HISTORY

Chronic Afferent Loop Syndrome

Three patients with chronic afferent loop syndrome (Cases 1-3) were elderly and presented with a history of intermittent epigastric pain, weight loss, and episodic nausea and vomiting after meals, which became worse later in the day.

All three patients had undergone a Billroth II partial gastrectomy with an antecolic anastomosis nine, six and one year previously. Originally two of the patients had had a gastroenterostomy complicated by a perforated stomal ulcer; subsequently the gastrectomy had been done because of the ulcer.

On radiographic examination we demonstrated an air-fluid level in a dilated loop of small intestine in one and evidence of a dilated jejunal loop in all three.

Case 1.—P.M., a 67-year-old man, was first admitted on January 10, 1967, with mild, dull, steady epigastric pain and bilious vomiting after meals for six months. The symptoms became worse towards the end of the day and vomiting usually occurred in the evenings. He had no history of weight loss.

A gastroenterostomy for duodenal ulcer had been performed elsewhere in 1954 and later a jejunal enteroenterostomy had been done. In 1958 a stomal ulcer perforated and he underwent partial gastrectomy with Billroth II, antecolic, gastroenterostomy reconstruction at another hospital.

On admission to St. Joseph's Hospital, the abdomen was soft and not tender. Prominent peristaltic waves were visible in all quadrants

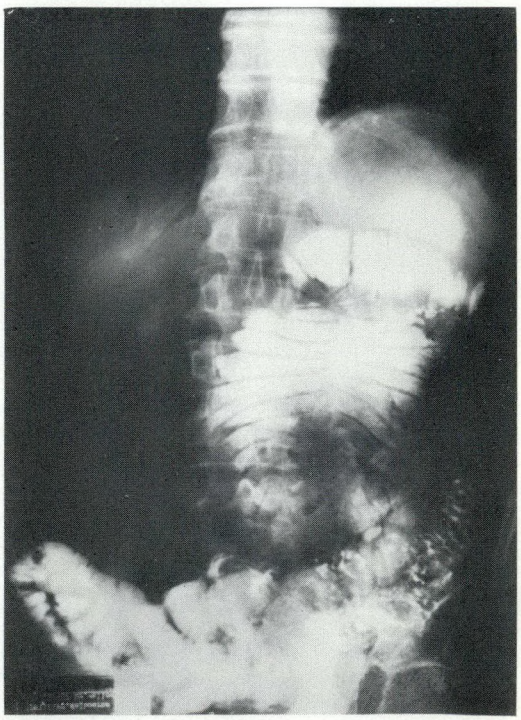

Fig. 1.—Case 1. Barium meal examination shows a markedly dilated afferent loop with delayed emptying on follow-up films.

*From the Department of Surgery, St. Joseph's Hospital, 30 The Queensway, Toronto 156, Ont.

of the abdomen. Laboratory findings were unremarkable. Barium meal examination showed a markedly dilated afferent loop with delayed emptying on follow-up films (Fig. 1).

At laparotomy on January 23, 1967, he had a stenosis of the efferent loop at the site of the gastroenterostomy that accompanied the gastrectomy, with a markedly dilated blind pouch of the proximal loop where the previous enteroenterostomy had been done (Fig. 2).

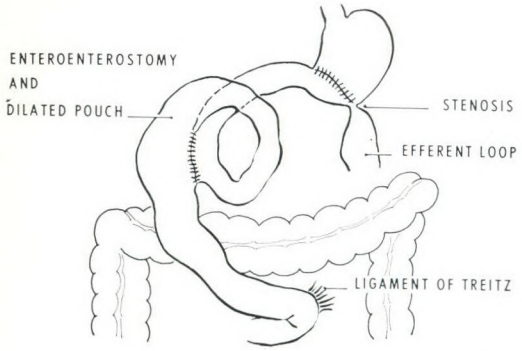

Fig. 2.—Case 1. Mechanism of obstruction.

The stenosis was relieved by an enteroplasty of the Heineke-Mikulicz type, with resection of the blind pouch and end-to-end anastomosis. Recovery was uneventful and on examination one year later, he had no symptoms.

Case 2.—M.S., a 76-year-old widow, was admitted on November 21, 1967, with severe, constant epigastric pain and vomiting of two weeks' duration. She had been well until one year earlier when she began to have crampy, postprandial, epigastric pain which was relieved by vomiting of food and bile. In 1961 she had had a partial gastrectomy and Billroth II antecolic gastroenterostomy for a benign gastric ulcer.

The right upper quadrant of the abdomen was tender and rigid, and bowel sounds were absent. Her leukocyte count and hemoglobin were normal. Barium meal examination demonstrated delayed emptying of the proximal loop with stenosis at the site of the gastroenterostomy (Fig. 3). Nasogastric suction relieved her symptoms temporarily but they recurred after a short period.

On November 27, 1967, she developed severe bronchopneumonia and died three days later. At postmortem examination she had a severe, confluent bronchopneumonia. A stomal ulcer and stenosis of the proximal loop at the site of the gastroenterostomy had produced chronic obstruction (Fig. 4).

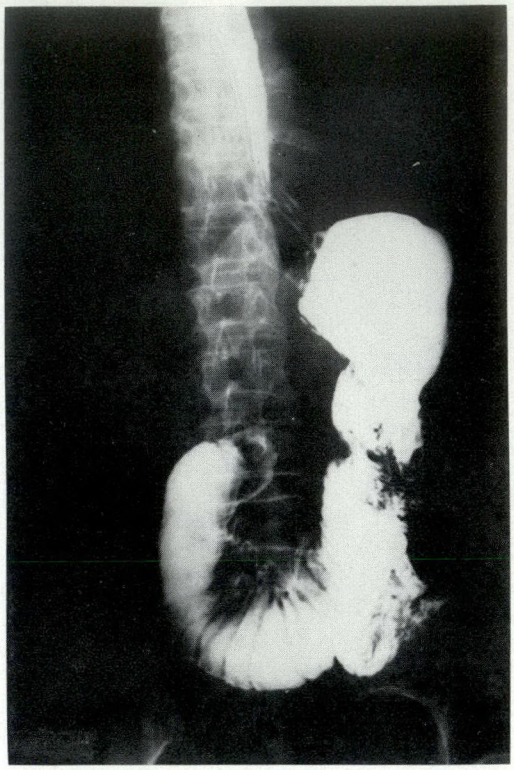

Fig. 3.—Case 2. Barium meal examination shows stenosis at the site of the gastroenterostomy with delayed emptying on follow-up films.

The intermittent, crampy, postprandial epigastric pain of one year's duration, which was relieved by vomiting of food and bile, was typical of afferent loop obstruction secondary to stomal ulceration.

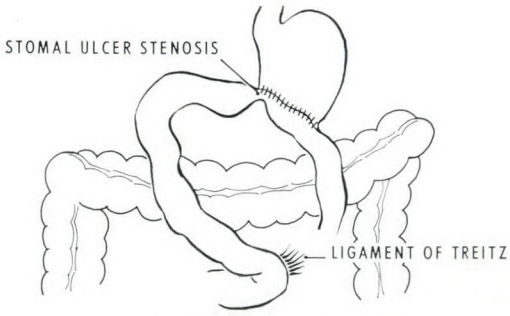

Fig. 4.—Case 2. Mechanism of obstruction.

Case 3.—H.S., a 71-year-old man, was admitted in August 1962 with weight loss, episodic nausea and bilious vomiting of approximately five months' duration.

He had been admitted to St. Joseph's Hospital in 1958 because he had perforation

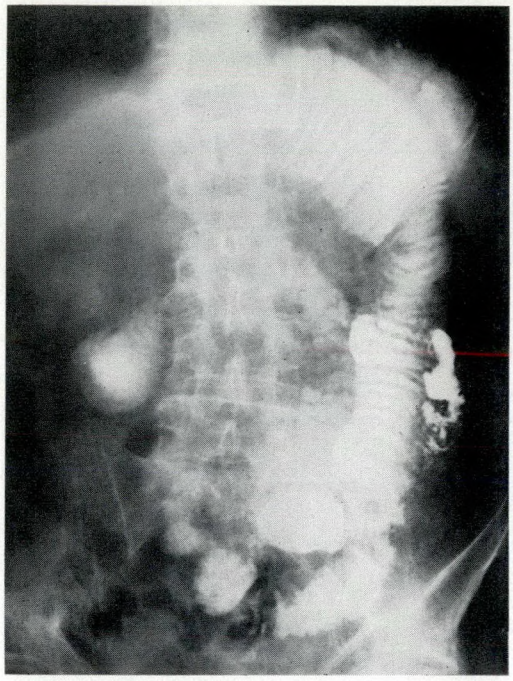

Fig. 5.—Case 3. Barium meal examination shows a dilated redundant loop.

of a duodenal ulcer; it was closed by an omental patch. After operation gastric emptying was never adequate and he had a severe upper gastrointestinal hemorrhage. Because of his age and critical condition, we did a simple gastroenterostomy with some misgivings. He made a satisfactory recovery except that the wound became infected and he developed a large ventral hernia.

Between 1958 and 1962 the ventral hernia was repaired several times. He had a partial gastrectomy with Billroth II, antecolic gastroenterostomy in early 1962 after a stomal ulcer perforated.

On this final admission in August 1962, because of his weight loss, episodic nausea and bilious vomiting, we did an upper gastrointestinal series, which showed an obstructed segment of jejunum about 20 cm. in length (Fig. 5). The diagnosis of afferent loop obstruction was thus made.

At operation a redundant and markedly dilated loop of afferent jejunum (Fig. 6) was excised and an end-to-end anastomosis done. The length of the afferent loop in this case gave rise to the chronic obstruction and dilatation. Probably he had recurrent volvulus which, fortunately, never produced complete obstruction or strangulation.

After operation, this patient did well and, on follow-up examination six years later, he had no residual gastric complaints.

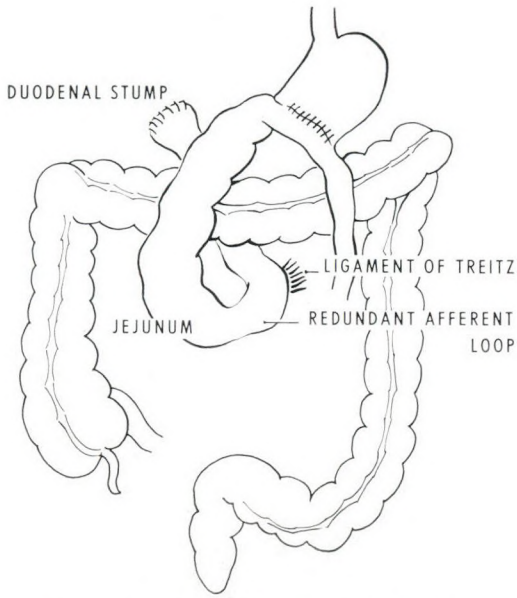

Fig. 6.—Case 3. Mechanism of obstruction.

Acute Afferent Loop Syndrome

Two patients (Cases 4 and 5) had the delayed form of the acute afferent loop syndrome with the sudden onset of severe, constant epigastric pain. Both had some evidence of acute pancreatitis and one had evidence of obstructive jaundice. Both had undergone a Billroth II partial gastrectomy with an antecolic anastomosis 9 and 11 years earlier. One patient had had volvulus of a redundant afferent loop, which was reduced at operation.

On radiographic examination these patients had a dilated loop of small intestine, which was interpreted as jejunum. Both underwent laparotomy without delay.

Case 4.—H.M., a 50-year-old woman, was admitted on June 25, 1967, with a history of constant, upper abdominal pain, jaundice, anorexia and constipation, but no vomiting. Elsewhere, in 1958, she had had a partial gastrectomy with Billroth II antecolic gastroenterostomy for peptic ulcer. She had had a cholecystectomy at the same time.

On admission, the patient's oral temperature was 98.6° F., respirations 18/min., pulse rate 116/min. and blood pressure 140/90 mm. Hg. Her skin was markedly icteric. Her abdomen was distended with maximum tenderness in

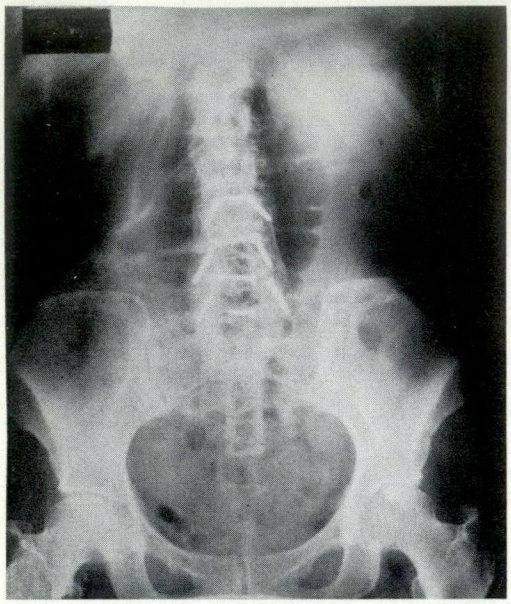

Fig. 7.—Case 4. Plain, supine film of the abdomen shows a dilated loop of small bowel.

the left lower quadrant. Bowel sounds were decreased, but no definite palpable mass was present.

Her hemoglobin, leukocyte count and blood urea nitrogen were normal. An emergency flat plate of the abdomen showed a dilated loop of small bowel (Fig. 7).

Because she improved very little after being on nasogastric suction overnight, she was taken to the operating room for laparotomy. The afferent loop had twisted into a volvulus and was gangrenous (Fig. 8). She had generalized bile peritonitis and the pancreas was markedly edematous.

We excised the necrotic segment between the ligament of Treitz and the stomach, and closed the duodenum at the duodenojejunal junction. The junction of afferent jejunal loop and the stomach was closed, leaving the gastric remnant emptying directly into the efferent jejunal loop. A Roux-en-Y loop was constructed 18 inches from the gastroenterostomy and an end-to-side, retrocolic duodenojejunostomy performed (Fig. 9).

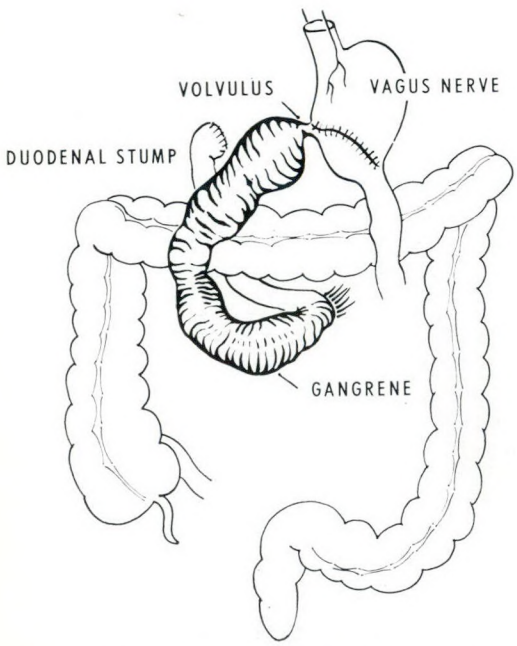

Fig. 8.—Case 4. Mechanism of obstruction.

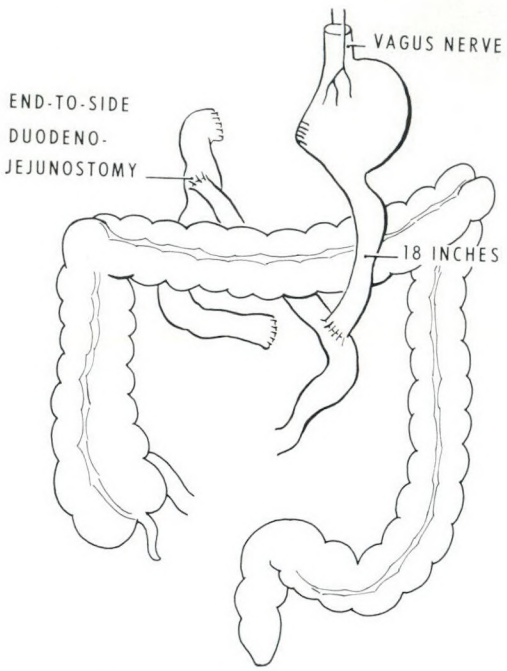

Fig. 9.—Case 4. Operative correction.

After operation her recovery was uneventful. At present she is being treated for esophageal achalasia, a condition that her family physician had noted before operation. The patient has gained weight and feels better than she did before the original partial gastrectomy (Fig. 10).

Case 5.—O.B., a 72-year-old man, was admitted on May 20, 1967, because of constant, generalized, severe epigastric pain and bile-stained vomiting of about 17 hours' duration.

At this hospital in August 1956 he had had a partial gastrectomy with Billroth II, antecolic gastroenterostomy for a chronic gastric ulcer.

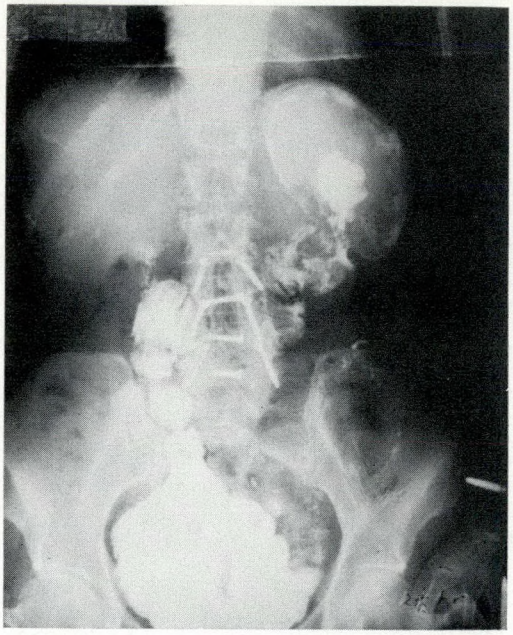

Fig. 10.—Case 4. Barium meal examination six months after operation.

After operation he had been treated for recurrent, upper abdominal pain and a macrocytic anemia. In 1965 he had had a simple reduction of a volvulus of the afferent loop.

His leukocyte count and hemoglobin were normal and his serum amylase was 453 Somogyi units. Emergency radiographs did not contribute any useful information. While still in the emergency room, he became hypotensive and was immediately transferred to the operating room for laparotomy. He had a recurrent volvulus of the proximal loop with marked surrounding edema (Fig. 11). The volvulus was reduced and, since the bowel was considered to be viable, an enteroenterostomy was done.

After operation the patient remained in critical condition and had to be maintained by blood transfusions, steroids and isoproterenol. Seven days later he developed a severe, upper gastrointestinal hemorrhage and required many blood transfusions.

Sixteen days later he began to have foul-smelling, dark-brown vomitus with similar drainage from the incision, which we considered indicated that the bowel was necrotic. He deteriorated rapidly and died the same day before we could get him ready for laparotomy.

At autopsy, the duodenal stump had perforated and he had generalized peritonitis and septicemia. The site of the gastrointestinal bleeding was never determined. We believe the duodenal stump perforated because the almost gangrenous afferent loop had not been adequately decompressed.

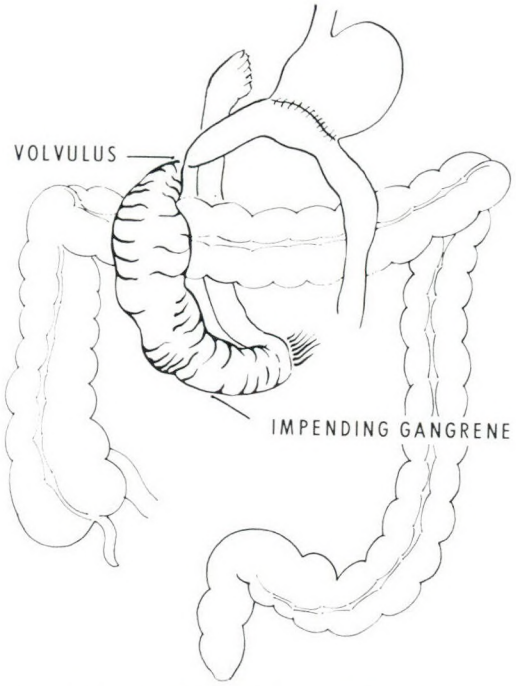

Fig. 11.—Case 5. Mechanism of obstruction.

Incidence

The incidence of afferent loop syndrome after gastroenterostomy alone or when associated with gastrectomy has been estimated to be between 5% and 20%.[2] During the past six years at St. Joseph's Hospital we have encountered five patients with this syndrome.

Etiology

Afferent Loop Syndrome After Antecolic Gastroenterostomy With or Without Partial Gastrectomy

Many factors play a part in acute and chronic afferent loop obstructions, but our five patients all had had a Billroth II partial gastrectomy with an antecolic anastomosis. All had a redundant proximal loop, which may give rise to kinking, intussusception or volvulus, either acute or chronic.

In the acute afferent loop syndrome there is complete obstruction which may progress to strangulation and gangrene. In

this closed-loop obstruction the bowel may eventually perforate giving rise to generalized peritonitis.

In the chronic syndrome arising in association with antecolic anastomosis the afferent loop seems to kink near the junction of the loop and the stomach giving rise to chronic intermittent obstruction. This obstruction leads to distension and thickening of the bowel which cause further episodes of kinking or perhaps intussusception or volvulus. At this stage the patient complains of intermittent, crampy epigastric pain, which is worse after meals and later in the day, and is frequently relieved by the vomiting of food and large quantities of bile.

At this stage the chronic syndrome may be suddenly converted into the acute form when acute obstruction of the afferent loop develops which, if untreated, may progress to gangrene of the bowel.

Afferent Loop Syndrome After Retrocolic Gastroenterostomy With or Without Partial Gastrectomy

When an afferent loop obstructs in a patient with a retrocolic anastomosis, two complications threaten: if the closure of the transverse mesocolon is incomplete an internal hernia may develop or, conversely, if the closure of the mesocolon around the loop is excessively tight, the bowel may be stenosed. Either may give rise to acute or chronic proximal loop obstruction.

The Role of Stomal Ulceration in the Afferent Loop Syndrome

After either antecolic or retrocolic reconstruction a stomal ulcer may develop and associated edema may obstruct the afferent loop and give rise to the chronic syndrome.

As the loop dilates and hypertrophies during chronic obstruction, it is more liable to kink or twist and, hence, convert suddenly to the delayed acute syndrome with all its consequences.

Pathophysiology

Acute

The *acute afferent loop syndrome* (Fig. 12) may manifest itself immediately after operation. In these instances, the afferent loop distends and the duodenal stump may leak or perforate.

In the *delayed acute syndrome* the afferent loop symptoms may be preceded by bleeding or perforation of a stomal ulcer. Afferent loop obstruction, pancreatitis and ascending cholangitis may complicate the clinical presentation. If afferent loop distension is progressive the bowel becomes ischemic, the afferent loop becomes gangrenous and subsequently perforates with generalized peritonitis.[5] If the developing syndrome is recognized early enough, operation at this stage may well be successful.

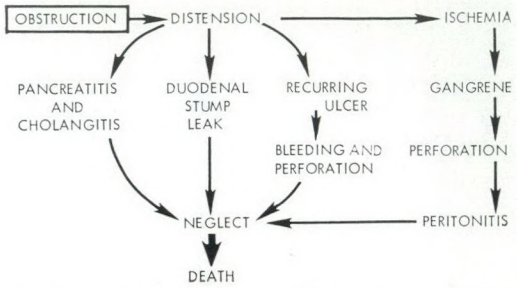

Fig. 12.—Pathophysiology in the acute syndrome.

Chronic

Chronic afferent loop syndrome (Fig. 13) will manifest itself as a high, small intestinal obstruction and, in some cases, with an added blind loop syndrome. Stagnation in the incompletely obstructed afferent loop alters the bacterial flora with one of several consequences: vitamin B_{12} deficiency may develop; deamination may lead to protein deficiency which, in turn, leads to either pancreatic or hepatic insufficiency; altered bacterial growth may

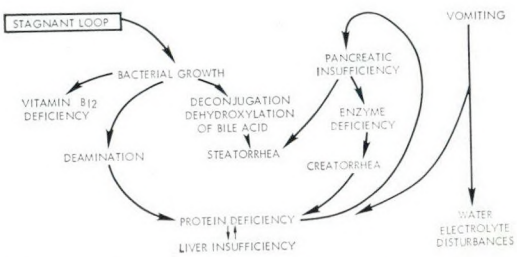

Fig. 13.—Pathophysiology in the chronic syndrome.

cause deconjugation and dehydroxylation of bile acids and, because of this, steatorrhea develops.[6]

The small-bowel obstruction, vomiting, and the above-mentioned steatorrhea and diarrhea in time produce fluid and electrolyte imbalances; hence, when the patient is seen, he is chronically ill and dehydrated.

Discussion

Diagnosis before laparotomy was difficult. However, the most important factor in recognizing the syndrome was to be aware of it. To prevent gangrene of the intestine, the surgeon must differentiate the acute afferent loop syndrome from acute pancreatitis due to other causes. Of our five cases, two with acute afferent loop obstructions (Cases 4 and 5) had evidence of acute pancreatitis at the time of laparotomy.

Both acute and chronic syndromes were seen mainly in elderly patients. This suggests that, as in volvulus of the colon, the loss of normal tissue support is a contributing factor. Our patients were 76, 72, 71, 67 and 50 years of age. For a person of her age, the youngest patient had a marked loss of normal tissue elasticity.

Two patients (Cases 1 and 3) had both a stomal ulcer perforation and a long afferent loop; the latter probably caused the afferent loop syndrome.

Various operative procedures used in the treatment of afferent loop syndrome have been summarized by Herrington.[2] The most widely used procedures are conversion of Billroth II to Billroth I, Roux-en-Y anastomosis and enteroenterostomy.

In our series two of the three patients with the chronic syndrome were operated upon (Cases 1 and 3). In one, the stenosis was relieved by an enteroplasty and in the other, by resection of a redundant loop of afferent jejunum. In both, these procedures relieved the obstruction and on follow-up both had a satisfactory result.

In one patient with the acute syndrome (Case 5) we reduced the recurrent volvulus and did an enteroenterostomy; however, this patient died later with evidence of persistent afferent loop obstruction and perforation of the duodenal stump. We made an error in judgment concerning the viability of the involved afferent loop and the adequacy of decompression. At autopsy the perforation was secondary to inadequate decompression of an almost gangrenous afferent loop.

The other patient with the acute syndrome (Case 4) had gangrene of the proximal loop and, although she was not operated upon until one week after her symptoms began, she survived.

In analyzing our Case 4 and the survivor reported by Sisler, Haims and Spencer,[3] we concluded that when a patient has gangrene or impending gangrene of the afferent loop, the necrotic segment should be excised between the ligament of Treitz and the stomach, and the duodenum closed at the duodenojejunal junction. The junction of the afferent jejunal loop and stomach is closed, leaving the gastric remnant emptying directly into the efferent jejunal loop. A Roux-en-Y loop is constructed about 18 inches from the gastroenterostomy and an end-to-side, retrocolic duodenojejunostomy performed. This is a relatively minor procedure compared to the Whipple operation which must be performed if the duodenum is not viable. There is much less chance of progressive gangrene proximal to the ligament of Treitz after decompression because of the double blood supply of the duodenum. This procedure is physiologically more sound than an enteroenterostomy if there is any question as to the viability of the acutely obstructed afferent loop. To prevent stomal ulceration vagotomy can also be done at the same time or as a secondary procedure if the previous gastrectomy is inadequate or if gangrene of the afferent loop has developed after gastroenterostomy alone. However, as suggested by others,[2] patients with unequivocal gangrene of the duodenum should have the Whipple procedure.

According to Sisler, Haims and Spencer[3] only one patient out of five with proximal loop gangrene survived.

Summary

Afferent loop syndrome, an uncommon complication of gastroenterostomy, either alone or when combined with a Billroth II

gastrectomy, consists of a closed-loop obstruction of the afferent jejunal loop. The acute syndrome may manifest itself either immediately after operation or may be delayed in onset; the chronic form presents with recurrent episodes usually taking place over a more prolonged period.

Five patients with afferent loop obstruction, encountered at St. Joseph's Hospital, Toronto, are presented with emphasis on the important factors in their recognition. The incidence and etiological factors are discussed. The pathophysiological details of the acute and chronic syndrome are discussed and details of corrective operations outlined.

Where there is gangrene or impeding gangrene of the proximal loop, duodenojejunostomy with excision of the loop between the ligament of Treitz and the gastrojejunostomy is the treatment of choice. This is a relatively minor operation in comparison with a Whipple procedure and is anatomically more sound than an enteroenterostomy.

References

1. Frey, C. F. and Coon, W. W.: Afferent loop obstruction, *Amer. J. Surg.*, **115:** 730, 1968.
2. Herrington, J. L., Jr.: Experience with surgical management of afferent loop syndrome, *Ann. Surg.*, **164:** 797, 1966.
3. Sisler, G. E., Haims, B. W. and Spencer, F. C.: Postgastrectomy afferent loop volvulus and gangrene. A late complication simulating gastritis, *Amer. J. Surg.*, **114:** 932, 1967.
4. Southam, J. A.: Acute afferent loop obstruction, *Ann. Surg.*, **165:** 323, 1967.
5. Hardy, J. D.: Complications of gastric resection. *In:* Complications in surgery and their management, 2nd ed., edited by C. P. Artz and J. D. Hardy, W. B. Saunders Company, Philadelphia, 1967, p. 429.
6. Jorden, P. H., Jr.: Physiology of the small intestine, *Surg. Gynec. Obstet.*, **124:** 1331, 1967.

Résumé

Le syndrome de l'anse afférente, complication rare d'une gastro-entérostomie, seule ou associée à une gastrectomie de Billroth (2e procédé), consiste en une obstruction par bouclage serré de l'anse afférente du jéjunum. La forme aiguë peut se manifester soit immédiatement après l'opération, soit avec un temps de latence; la forme chronique est caractérisée par des épisodes récidivants qui s'étalent généralement sur une période plus prolongée.

Les auteurs en présentant cinq cas semblables, tous rencontrés à l'Hôpital St-Joseph de Toronto, soulignent les facteurs importants de leur découverte. Ils exposent la fréquence de ce type de syndrome et ses facteurs étiologiques. Ils donnent les détails physiopathologiques des formes aiguë et chronique ainsi que la description des opérations correctrices.

En présence de gangrène ou de menace de gangrène de l'anse proximale, le traitement par excellence consiste à pratiquer une duodénojéjunostomie comportant l'excision de l'anse entre le ligament de Treitz et la gastrojéjunostomie. Cette opération est relativement mineure par rapport à l'opération de Whipple et, par ailleurs, elle est plus logique, au point de vue anatomique, qu'une entéro-entérostomie.

HYPERBARIC OXYGEN IN EXPERIMENTAL BURNS

A beneficial effect of hyperbaric oxygenation on the course of experimental shock has been reported by several investigators. In a first series of experiments, the authors subjected rats to a hot water burn covering 75% of the body surface. Following the burn, some were treated with high pressure oxygen (HPO), some with HPO and fluid administration, and some with HPO and intravenous THAM buffer. The best survival rate was obtained in the group given THAM and exposed to HPO for one hour every other day, but the results were not convincing. In a second group of experiments, a 30% burn and the effect of HPO one hour every other day, the administration of THAM, and the administration of penicillin and colimycin were investigated, each agent being administered either alone or in combination with one or both of the others. A significant prolongation of the survival time was observed with the administration of THAM and an even better survival rate was obtained by the administration of HPO, THAM and the antibiotics. Exposure to HPO alone decreased the survival rate.—Benichoux, R. *et al.*: L'oxygène hyperbare dans le traitement des brûlures graves expérimentales, *J. Chir. (Paris)*, **96:** 445, 1968.

"TRYPTIC ENTERITIS": ITS ROLE IN THE PATHOGENESIS OF STRESS ULCER AND SHOCK*

GUSTAVO BOUNOUS, M.D.,† *Sherbrooke, Que.*

EARLY in the nineteenth century, Dupuytren[1] described the visceral changes seen at autopsy in patients who died of severe burns after a protracted period of shock. The gastric lesion was characterized by multiple, small mucosal ulcers while, in many cases, the intestine showed extensive areas of mucosal necrosis and hemorrhage. In the years that followed, Cumin,[2] Swan,[3] Curling[4] and Billroth[5] described small areas of erosion and necrosis in the gastrointestinal tract following traumatic or septic episodes.

The main purpose of the work described in this paper was to investigate the relationship between mucosal ulcers in the stomach and the intestine, and examine their possible role in the pathophysiology of shock.

MUCOSAL LESIONS IN SHOCK

The gastroduodenal erosions are usually well circumscribed, multiple, superficial and show no inflammatory reaction. Although authorities agree on the systemic conditions in which the mucosal ulcer develops, its pathogenesis is not well understood. While the gastric or duodenal stress ulcer is well recognized, the concomitant intestinal lesion has been neglected. Recently, however, non-embolic hemorrhagic enteritis has been reported in conditions analogous to those in which gastric ulcers develop.[6-41] Often both lesions are found together at autopsy.[1, 3, 8-10, 12, 14-16, 18, 19, 24, 28-32, 35, 40] The intestinal lesion, which is initiated by ischemic anoxia, begins in the epithelial cells at the tip of the villi. In the early stages, seen better at biopsy in the experimental animal, mucin is lost rapidly and the microvilli are shredded. Vacuoles form in the cytoplasm, which fragments, and finally part of the cell is shed into the lumen, leaving behind streamers of cytoplasm (Fig. 1). During this process, the

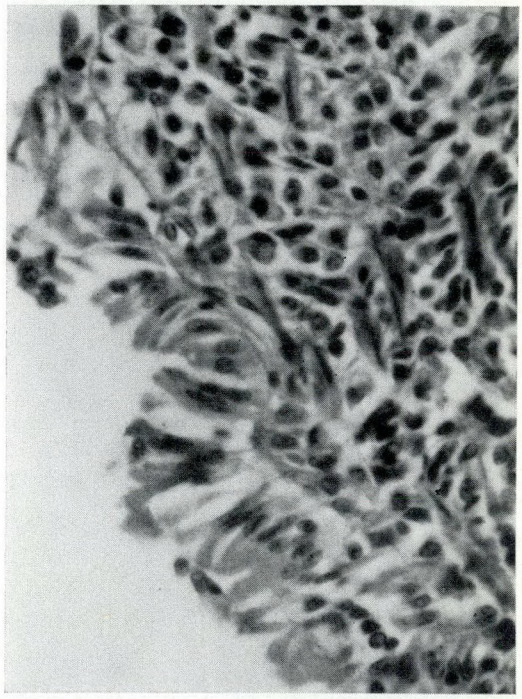

Fig. 1.—Mucosa of the ileum—dog 7369. Biopsy two hours after occlusion of the superior mesenteric artery, fixed *in vivo,* shows fragmentation of the epithelium (H & E).

villus may be totally denuded, remnants of cytoplasm may coalesce to form bridges or adjacent villi may fuse (Fig. 2). If the entire epithelial lining is lost, massive hemorrhagic enteritis may develop and the entire villus is destroyed (Fig. 3) or several adjacent villi may fuse, forming a block of tissue which later is covered by flat or cuboidal cells (Fig. 4). Because the intestinal lesion is usually associated with serious systemic disease, death may interrupt the evolution of this process at any stage. Necrosis of the intestinal epithelium occurs early in shock and, in the experimental animal at least, provides the first gross histological evidence of systemic hypotension. Such necrosis closely re-

*From the Department of Surgery, University of Sherbrooke, Centre Hospitalier Universitaire, Sherbrooke, Que.

This work was supported by the Medical Research Council of Canada. Part of the work was performed at the University Surgical Clinic of the Montreal General Hospital, Montreal, Que.

†Associate Professor of Surgery, University of Sherbrooke, Sherbrooke, Que. Research Associate, Medical Research Council of Canada.

Fig. 2.—Mucosa of the ileum—dog 7511, fixed *in vivo*. Cytoplasmic bridges are seen between adjacent villi (H & E).

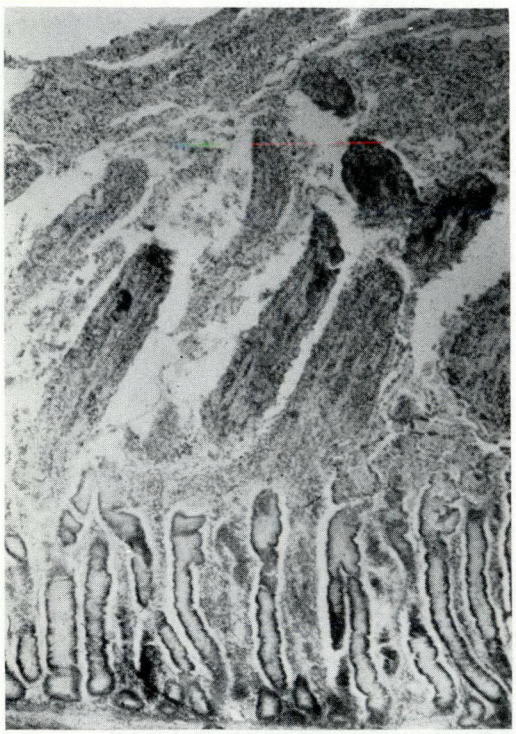

Fig. 3.—Mucosa of the ileum—dog 7377, fixed two hours after death—showing massive enteritis (H & E).

sembles normal postmortem autolysis.

Hypotension, ischemia and various forms of injury act on energy production in the lining epithelium and destroy the continuity of the mucous shield and cellular membranes. In 1964 and later,[42-44] we demonstrated that intraluminal, pancreatic, proteolytic enzymes digested the exposed structures of the mucosa—a process marked by the rapid dissolution of epithelial cells, lymphocytes and macrophages, often with hemorrhage from the exposed vascular network.

Fig. 4.—Mucosa of the ileum—dog 7511, fixed *in vivo*. There is fusion of adjacent villi which are covered with flat cells (H & E).

Tryptic Enteritis

Because the role of trypsin in this second phase of the syndrome has been repeatedly confirmed,[45-53] our original term "tryptic enteritis" seems appropriate, particularly when applied to the alterations in the lamina propria. The second phase involves the villus stalk, the mucosa may become dark-red in scattered, irregular patches or, in more severe cases, in long, confluent stretches. It should be noted that this change bears no relation to the distribution of any particular branch of the mesenteric

arteries. In addition there is no inflammatory reaction and the muscular and serosal layers are often intact.

Its pathogenesis and the frequency of this intestinal lesion in shock suggest that the hypotension initiates it, that it may contribute to the gradual deterioration of the cardiovascular system and may lead to irreversible shock. Lillehei[54] increased survival by perfusing the superior mesenteric artery during hypovolemic shock. Furthermore, a relationship has been demonstrated between decreased mesenteric oxygen consumption and the severity of the associated shock.[55-58] Also a relationship exists between the magnitude of intestinal mucosal necrosis and the outcome of shock.[59, 60] Finally, if the bowel is denervated and protected in other ways, survival after experimental shock also increases.[59, 61, 62]

In the normovolemic phase of shock, "shock toxin", which originates in the intestinal tract, probably contributes to the circulatory derangement. This toxin appears to be a small molecule, not of bacterial origin, which depresses the blood pressure and the reticuloendothelial system.

The preparation known as "experimental non-occlusive mesenteric ischemia"[53] provides an excellent model by which to study the "intestinal factor" separately. In the dog, by clamping the superior mesenteric artery for two hours, one can reproduce the intestinal damage seen in dogs after four hours of hypovolemic hypotension (40 mm. Hg). The intestinal lesion thus produced is limited to the superficial mucosa and, once the clamp is removed, the circulation is re-established and all vessels open to their smallest measurable diameter (25μ to 50μ).

The Present Study

In the study described below, we recorded the hemodynamic consequences of mesenteric ischemia and the concomitant release of intestinal enzymes. Our purpose was not to demonstrate that the intestine is either the sole or even the principal source of toxins in shock, but to study the conditions that facilitated the evolution of the ischemic mucosal necrosis. Our previous work[59] indicated that some of these conditions are related to diet and digestion because the lesions may be favourably modified before shock by feeding the experimental animal an "elemental diet". This is the point: the intestinal factor is of vital interest because it can be manipulated by prophylactic treatment. Because of this, the intestine has a special status among the other "shock organs". The present study shows that, if we inhibit the pancreatic trypsin in the chyme before we occlude the superior mesenteric artery for two hours, the subsequent mucosal necrosis is much less severe.

Material and Methods

The studies were done on 28 adult mongrel dogs weighing from 17 to 22 kg. They were given pentobarbital (Nembutal), 25 mg./kg., intravenously and this was supplemented if required. Food was withdrawn 18 hours before the experiment. All animals were autopsied as soon as possible after death or when they were killed—48 hours after the onset of intestinal ischemia. These latter animals were considered to be survivors.

The superior mesenteric artery was approached through a midline abdominal incision, to reach it near its origin from the aorta. After the artery was clamped, occlusion was confirmed by observing that the gut-wall vessels did not pulsate and that pulsatile flow returned after release. Arterial blood samples were drawn into a heparinized syringe from a catheter in the femoral artery: 40 ml. before occlusion, 60 minutes after the clamp was removed and again before the dog was killed.

Because the gut usually contains only a few millilitres of chyme after an 18-hour fast, we introduced 40 ml. of Ringer's lactate into the duodenum through a 20G needle. This fluid was gently milked down and, about one hour later, the chyme obtained from the whole ileum was withdrawn through a 16G needle. This usually produced 15 to 20 ml. of chyme for the various chemical analyses. A second sample of chyme was obtained in the same manner 60 minutes after the clamp was removed. The following determinations were done: serum hemoglobin was measured according to the method of Beau.[63] Acid phosphatase,[64] serum lipase[65] and serum amylase[66]

were determined using diagnostic kits from Sigma Chemical Co., St. Louis, Missouri. Beta-glucuronidase was estimated according to the method previously described.[67] Trypsin in the chyme was measured spectrophotometrically using the method of Lundh,[68] with n-bensoyl-arginine-ethyl ester as substrate with 0.05 M Tris buffer containing 0.02 calcium chloride. The enzymatic activity, expressed as mg./ml., refers to standard reference curves with known amounts of enzymes. Trypsin was determined as an index of the concentration of pancreatic proteolytic enzymes because trypsin and chymotrypsin follow each other in a fairly constant ratio.[69] RNAase (ribonucleic acidase) was estimated by a method previously described.[70]

The same procedures were done and the same determinations made in another 14 dogs (Group 2) except that 1 g. of ovomucoid trypsin inhibitor (Mann Research Laboratory, New York, N.Y.) was dissolved in the Ringer's lactate introduced in the duodenum.

Evaluation of Mucosal Change

Even immediately after sacrifice the condition of the mucosa cannot be evaluated on the basis of colour changes. After two hours of ischemia the epithelium loses almost all its mucous coat—a condition that persists for several days because even the newly formed flat cells are mucin free. Under these conditions reactive hyperemia, which also persists for a long time, is interpreted as colour change even if there is neither epithelial necrosis nor interstitial hemorrhage on histological section. Furthermore, our experience, like that of others,[71] suggests that, while reactive hyperemia occurs regularly in most tissues, it does so irregularly in the intestine. For example, after a period of ischemia, a patch of red mucosa may represent the following histological changes: denuded villus with hemorrhage (Fig. 3); fragmented, shrunken or flat epithelium with loss of mucin and reactive hyperemia (Fig. 5); or near-normal epithelium with loss of mucin and severe hyperemia. Also, if epithelial necrosis is not accompanied by congestion or hemorrhage, the mucosa may appear normal on direct observation.

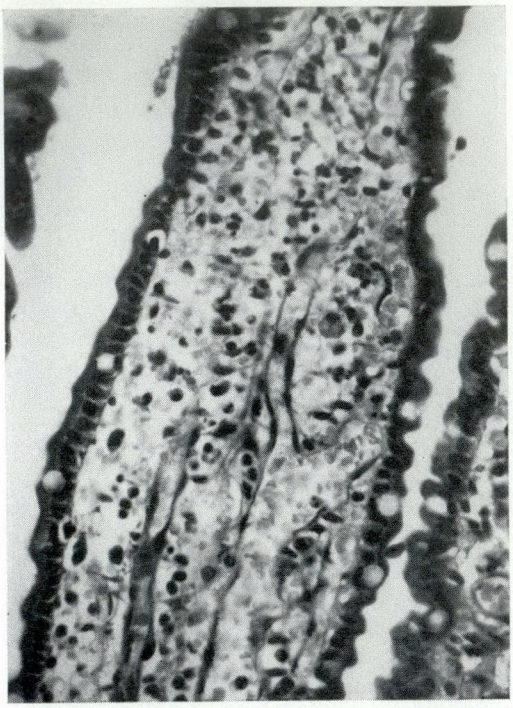

Fig. 5.—Mucosa of the ileum—dog 7621, fixed *in vivo*. The epithelium is cuboidal, the mucin is reduced and the vessels are dilated (H & E).

For all these reasons we abandoned the classical macroscopic description of the mucosa, but instead use the histology of the tissue fixed in 10% formalin at the time of sacrifice (Tables I and II). Ten specimens were taken, approximately 12 cm. apart, over an area extending distally from the ligament of Treitz to about 60 cm. from the ileocecal valve in the territory of the superior mesenteric artery. Each specimen was cut transversely so that the villus could be examined longitudinally, each section showing 200 to 300 villi. The final descriptions of the lesions in Groups 1 and 2 (Tables I and II), which are based on observations of approximately 3000 villi, refer to the lining epithelium and the lamina propria. When the extent of the lesion is given as a percentage, this indicates the percentage of the villus involved from the tip downwards.

Hemodynamic Studies

Cardiac output was measured by the dye dilution technique using a Gilford photoelectric densitometer Model 103-R

TABLE I.—Pathological Changes in Group 1 (Controls)

Dog no.	Lining epithelium	Lamina propria	Outcome
7352	Total denudation from tips to crypts	Hemorrhages on the exposed surfaces, the denuded areas structureless	Died: 24 hr.
7357	Post mortem: massive hemorrhagic necrosis	—	Died: 36 hr.
7369	70% of villi denuded	40% of lamina propria structureless	Sacrificed: 48 hr.
7374	5% of the tips with vacuolized cells; 10% of villi fused together	Congestion	Sacrificed: 48 hr.
7377	Post mortem: hemorrhagic necrosis	—	Died: 36 hr.
7385	40% of villi fused with the tips covered by flat epithelial cells. 20% of the tips covered by flat cells	20% of lamina propria structureless; hyperemia	Sacrificed: 48 hr.
7399	10% of the tips covered by fragmented cells	Normal	Sacrificed: 48 hr.
7419	30% of the tips covered with fragmented cells	Structureless	Sacrificed: 48 hr.
7423	All villi fused together; covered on the surface by flat cells	Hemorrhagic and structureless	Sacrificed: 48 hr.
7511	15% of villi fused; covered on the surface by cuboidal cells; 5% of the tips covered by flat cells	Diminished cellular components	Sacrificed: 48 hr.
7523	Hemorrhagic enteritis	—	Died overnight
7540	25% of villi fused; 10% of the tips covered by cuboidal cells	Mild congestion; loss of cellular structure near tips	Sacrificed: 48 hr.
7544	30% of the tips covered by fragmented or cuboidal cells	Diminished cellular components	Sacrificed: 48 hr.
7551	90% of villi fused; covered by flat cells	Interstitial hemorrhage	Sacrificed: 48 hr.
7562	40% of tips denuded	Congestion; 40% of lamina propria with interstitial hemorrhage	Sacrificed: 48 hr.

and cardiogreen dye. Recordings were made on a Rectiriter (Texas Instruments, Inc.). The downslope of each dye curve was extrapolated to correct for recirculation and, by semilogarithmic re-plotting, the area under the dye curve was integrated. The cuvette was calibrated by passing samples of blood containing known concentrations of dye through the densitometer recorder system.

TABLE II.—Pathological Changes in Group 2 (Trypsin Inhibitor)

Dog no.	Lining epithelium	Lamina propria	Outcome
7598	10% of villi cuboidal cells; 5% of villi denuded	Normal; some hyperemia	Sacrificed: 48 hr.
7610	5% of villi fused by cytoplasmic bridges; 10% of villi cuboidal, fragmented cells; 10% of villi denuded	Normal	Sacrificed: 48 hr.
7621	40% of villi fused; 20% of villi covered by vacuolized, shrunken cells. Most of the tips covered by vacuolized cells	Marked hyperemia	Sacrificed: 48 hr.
7634	No signs of hemorrhagic enteritis	—	Died: 48 hr.
7639	No signs of hemorrhagic enteritis	—	Died: 24 hr.
7649	Massive hemorrhagic enteritis	—	Died: 24 hr.
7651	50% of the tips covered by flat or cuboidal cells; 5% of tips denuded; 15% of villi fused and covered by flat cells	Normal; mild hypermia	Sacrificed: 48 hr.
7657	20% of villi fused with cuboidal or flat cells on the surface; 80% of remaining tips covered by cuboidal, fragmented cells	Normal	Sacrificed: 48 hr.
7661	10% of the tips covered by fragmented cells	Marked hyperemia	Sacrificed: 48 hr.
7681	15% of villi fused; covered by cuboidal cells. Fragmented cells on the tips of 10% of villi	Hyperemia	Sacrificed: 48 hr.
7701	40% of villi fused through cytoplasmic bridges. Vacuolized, cuboidal cells on the surface	Mild hyperemia	Sacrificed: 48 hr.
7712	10% of villi fused through cytoplasmic bridges. Fragmented cells on 10% of villi	Normal	Sacrificed: 48 hr.
7693	Hemorrhagic enteritis	—	Sacrificed: 48 hr.

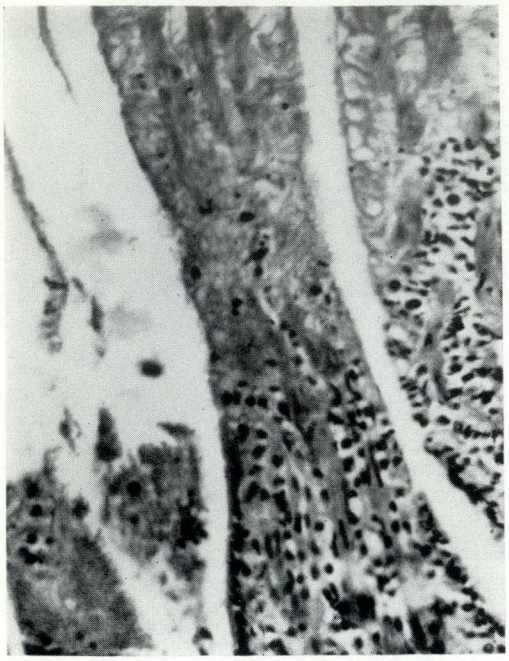

Fig. 6.—Mucosa of the ileum—dog 7369 (control), fixed *in vivo*. The cellular and vascular structures in the denuded part of the lamina propria have disappeared (H & E).

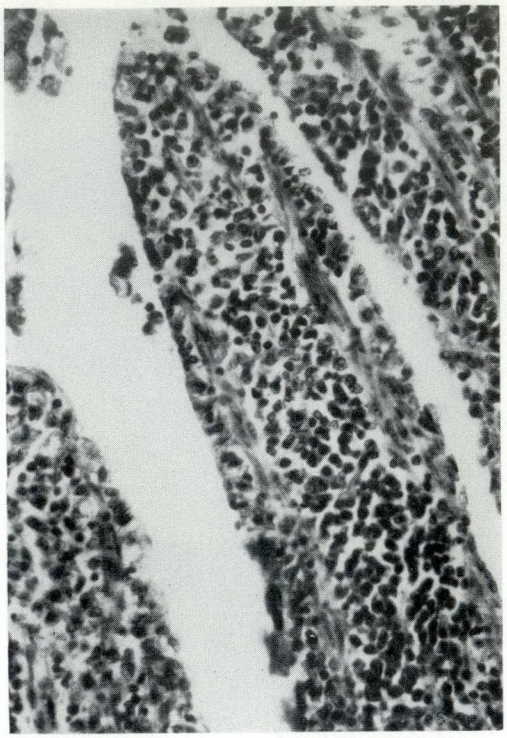

Fig. 7.—Mucosa of the ileum—dog 7610 (trypsin inhibitor), fixed *in vivo*—shows loss of epithelial lining with preservation of the cellular elements in the lamina propria (H & E).

Aortic blood pressure was recorded by introducing a polyethylene catheter in the aorta via the femoral artery. To measure the left ventricular end-diastolic pressure, another catheter, size 7F, was passed retrograde into the left ventricle. Both catheters were connected to Statham PD23 transducers. The reference point for all pressure measurements was the estimated level of the right atrium. A Grass Model 5 polygraph was used for recording.

Central venous pressure was measured as follows: an intradermic polyethylene catheter (PE-240) was passed 20 to 30 cm. through the right external jugular vein into the superior vena cava. The catheter was filled with heparinized isotonic glucose and connected to a tube from a plastic infusion set; this tube was fastened along a ruler whose zero point in each dog was the level of the control venous pressure. Once free flow was established, the correct position of the catheter was ascertained by demonstrating distinct respiratory fluctuations in the venous pressure. When the pressure determination was repeated after two days, the position of the apparatus and the zero level were unchanged.

Results and Discussion

Part I

In both groups of dogs two hours of ischemia produced significant anatomical damage in the intestinal epithelium (Tables I and II). In the treated group (Table II) the histological damage was less, particularly in the lamina propria (Figs. 6 and 7). Although the descriptions in Tables I and II refer to findings 48 hours after ischemia, previous biopsies showed that epithelial damage is visible as early as one hour after the onset of ischemia. Lysosomal enzymes may be released with cellular disruption or changes in cellular membrane permeability. Thus, it is not surprising to observe, one hour after "declamping", that the dry weight of the chyme has increased due to the addition of mucin and cellular debris. There is also a marked rise in acid phosphatase and, in Group 1 dogs, of beta-glucuronidase, which originates from the cytoplasm of dead cells (Table III). In control dogs, the activity of pancreatic

TABLE III.—Changes in Serum, Chyme and Gastric Juice After Temporary (Two-Hour) Occlusion of the Superior Mesenteric Artery in Group 1 (Controls)

		Hemoglobin (mg./100 ml.)	*Hematocrit (ml./100 ml.)*	*Acid phosphatase (units/ml.)*	*Ribonuclease ($\triangle E_{260}$/30 min. %)*	*Amylase (units/100 ml.)*	*Beta-glucuronidase (units/100 ml.)*	*Trypsin (mg./ml.)*	*Dry weight (%)*	*pH*
Serum	B	6.62 ± 2.21 (15)	42.91 ± 2.11 (11)	0.082 ± 0.010 (15)	149.92 ± 27.98 (12)	2600 ± 520 (11)	107.60 ± 44.17 (5)	—	—	—
	A_1	20.96 ± 4.02 (15)	53.54 ± 2.35 (11)	0.163 ± 0.036 (15)	237.83 ± 33.63 (12)	2523 ± 542 (11)	65.60 ± 27.78 (5)	—	—	—
	A_2	—	—	0.105 ± 0.028 (8)	190.25 ± 45.28 (8)	1633 ± 594 (6)	—	—	—	—
Chyme	B	—	—	7.963 ± 1.68 (11)	5207 ± 371 (9)	3204 ± 2471 (7)	95.90 ± 26.11 (10)	378.25 ± 83.18 (12)	3.336 ± 0.38 (11)	—
	A_1	—	—	26.36 ± 5.57 (11)	4916 ± 576 (11)	1499 ± 513 (7)	140.5 ± 38.79 (10)	42.66 ± 25.77 (12)	6.582 ± 0.83 (10)	—
Gastric juice	B	—	—	0.148 ± 0.064 (8)	—	—	57.22 ± 9.68 (9)	—	—	2.125 ± 0.337
	A_1	—	—	2.456 ± 1.01 (8)	—	—	180.25 ± 19.11 (8)	—	—	5.075 ± 0.555

B = control; A_1 = 1 hour after declamping; A_2 = 48 hours after declamping. All values are shown as mean ± standard error of mean (SEM). Number of animals is shown in brackets.

TABLE IV.—Changes in Serum, Chyme and Gastric Juice After Temporary (Two-Hour) Occlusion of the Superior Mesenteric Artery in Group 2 (Trypsin Inhibitor)

		Hemoglobin (mg./100 ml.)	*Hematocrit (ml./100 ml.)*	*Acid phosphatase (units/ml.)*	*Ribonuclease ($\triangle E_{260}$/30 min. %)*	*Amylase (units/100 ml.)*	*Beta-glucuronidase (units/100 ml.)*	*Trypsin (mg./ml.)*	*Dry weight (%)*	*pH*
Blood	B	4.32 ± 2.72 (12)	45.75 ± 4.81 (10)	0.08 ± 0.03 (13)	231.69 ± 21.73 (13)	4480 ± 30 (13)	—	—	—	—
	A_1	5.26 ± 2.16 (12)	54.3 ± 1.87 (10)	0.12 ± 0.04 (13)	238.76 ± 29.19 (13)	4170 ± 30 (13)	—	—	—	—
	A_2	—	—	0.13 ± 0.05	179.77 ± 36.90 (9)	—	—	—	—	—
Chyme	B	—	—	8.79 ± 2.39 (14)	3985 ± 281 (11)	1625 ± 561 (12)	114 ± 15.27 (11)	25.18 ± 6.25 (14)	3.19 ± 0.32 (14)	—
	A_1	—	—	15.46 ± 2.69 (14)	3635 ± 376 (11)	1265 ± 14.6 (12)	55.63 ± 12.80 (11)	12.80 ± 2.21 (14)	4.06 ± 0.45 (14)	—
Gastric juice	B	—	—	0.16 ± 0.09 (11)	179.4 ± 69.2 (11)	0	38.2 ± 10.3 (11)	—	1.44 ± 0.13 (10)	1.84 ± 0.24 (11)
	A_1	—	—	0.73 ± 0.27 (11)	1465 ± 500 (11)	0	90.2 ± 23.9 (11)	—	2.05 ± 0.29 (10)	3.70 ± 0.24 (11)

B = control; A_1 = 1 hour after declamping; A_2 = 48 hours after declamping. All values are shown as mean ± SEM. Number of dogs is shown in brackets.

trypsin in the chyme diminishes greatly after ischemia ($P<0.005$, Table III). This change is compatible with its suggested role in the digestion of the subepithelial structures of the villus. During the proteolytic process the substrate, by occupying the binding site on the enzyme, abolished the enzyme's action on other substrates. This explains why trypsin will not act upon the synthetic substrate used for its determination and why measurable tryptic activity is reduced. The importance of pancreatic, proteolytic enzymes in this proteolytic process is emphasized by their preponderance in the chyme; recently, it has been estimated that they represent two-thirds of the total proteolytic power.[72] *In vitro* experiments, in which chyme obtained after ischemia was incubated for four hours at 37° C. with known amounts of trypsin, have shown no significant antitryptic activity that would explain the observed drop in free trypsin. After comparing the histological findings and the biochemical data concerning the chyme in Groups 1 and 2 (Tables III and IV), we concluded that, to a certain extent at least, necrobiosis of the epithelium and subsequent shedding into the lumen after ischemia proceeds independent of the action of trypsin. Beta-glucuronidase in the chyme of Group 2 does not follow a consistent pattern after ischemia. In dogs in both groups, amylase and ribonuclease values in the chyme do not follow a consistent pattern after ischemia. However, it is interesting to note that the amount of acid phosphatase and percentage dry weight of the chyme are considerably greater after ischemia in Group 1 (<0.005) than in Group 2, where P values were not significant. The presence of trypsin must bring a faster dissolution of cellular elements.

An interesting corollary of the enzymatic changes in the chyme is the simultaneous changes seen in the gastric juices probably as an effect of reflux (Tables III and IV). In this particular study we did not attempt to assess the severity of the gastric lesions. We saw necrosis and erosions of the gastric mucosa in both groups although, grossly, these were markedly less severe in the treated dogs, both macroscopically and microscopically. These gastric lesions correspond well to the classical pathological definition of "stress ulcer"—multiple, small, superficial areas of erosion found almost anywhere in the gastric mucosa. In the control group (Table III) gastric analysis about one hour after "declamping" shows a constant rise of pH, acid phosphatase ($P<0.001$) and beta-glucuronidase ($P<0.05$). It is conceivable that these hydrolytic enzymes originated from the chyme where they had been found to be greatly increased. Other evidence, such as the presence of bile in the gastric juice, indicates that chyme is regurgitated into the stomach almost constantly. Although we made no special study of this subject, the reflux of hydrolytic enzymes and possibly potassium of intestinal origin into the stomach (Tables III and IV) during shock may contribute to these gastric erosions. To explain the digestion and reabsorption of mucin in the lower ileum, some workers have suggested that the intestinal epithelium must contain numerous mucopolysaccharidases. If these hydrolytic enzymes are present in the stomach in a free form, they may initiate changes in the gastric mucus, eventually leading to gastric necrosis. Indeed, the first histological change seen in the stomach after intestinal ischemia begins is loss of epithelial mucin. In the treated dogs the increase in acid phosphatase in chyme after ischemia is less significant than in control dogs, and the beta-glucuronidase activity does not increase; accordingly, the rise of these enzymes in the gastric juice is less significant when trypsin in the chyme is inhibited before ischemia (Table IV). Gastric erosions were also less frequent in the treated group.

These observations are consistent with the digestive action of trypsin upon the proteins of the ischemic intestinal mucosa. After the superior mesenteric artery has been occluded for two hours cytoplasmic enzymes and debris from the necrotic cells are released into the chyme. If trypsin is inhibited before clamping, the extent of cellular digestion is reduced.

Part II

The second part of this study was directed to the systemic effects of intestinal

TABLE V.—Hemodynamic Data in Group 1 (Controls)

Dog no.	A Control values				B End of occlusion				Hours after release: C 1 hour				D 48 hours			
	CO	BP	CVP	LVEDP	CO	BP	CVP	LVEDP	CO	BP	CVP	LVEDP	CO	BP	CVP	LVEDP
7347	140	125	—	0	100	110	—	−2	70	105	—	−4	—	—	—	—
7352	168	150	0	0	95	125	0.8	−9	75	95	−1.5	−14	—	—	—	—
7357	150	125	—	0	90	85	—	0	68	50	—	−5	—	—	—	—
7364	125	95	—	0	92	90	—	0	53	80	—	−3	—	—	—	—
7369	200	140	—	0	108	130	—	0	104	125	—	0	—	—	—	—
7372	200	145	—	0	138	130	—	−5	75	95	—	−10	—	—	—	—
7374	168	145	0	0	140	115	−0.8	0	84	95	−2.8	−2	—	90	−2	−2
7377	170	130	0	0	120	85	−1	−6	85	50	−2	−8	—	—	—	—
7385	198	125	0	0	140	110	−0.5	−3	149	100	−0.5	−5	148	100	—	—
7399	183	140	0	0	150	140	−1	−3	114	120	−1.2	−4	150	120	—	0
7419	168	120	0	—	128	120	−0.5	—	88	120	−1	—	130	90	−0.5	—
7423	145	125	—	0	125	115	—	−5	110	110	—	−5	145	110	—	0
7511	128	135	0	0	120	115	−0.5	−5	80	95	−2	−8	125	100	−2	−5
7523	155	140	0	0	120	120	−2	−5	100	110	−2.5	−9	—	—	—	—
7540	120	140	0	0	90	135	−1.2	−5	80	110	−2.5	−8	—	—	—	—
7544	150	140	0	0	135	140	−2.5	−12	75	120	−1.5	−10	98	120	−1.5	−10
7551	114	140	0	—	100	130	−0.8	—	89	125	−2	—	—	—	—	—
7562	125	140	0	0	95	140	−3	−7	58	105	−3.5	−8	65	100	−2	−15
Mean	156	133			116	118			86	100			123	103		
SEM	±6.57	±3.02			±4.72	±3.93			±5.35	±5.20			±11.83	±4.1		
Number	(18)	(18)			(18)	(18)			(18)	(18)			(7)	(8)		

CO A vs B $p < 0.001$ A vs C $p < 0.001$

CO = cardiac output (c.c./kg./min.); BP = mean arterial blood pressure (mm. Hg); CVP = central venous pressure (cm.H_2O); LVEDP = left ventricular end-diastolic pressure (mm. Hg).

ischemia. The severity of the hemodynamic changes was correlated with the extent of the mucosal damage; this, in turn, is influenced by the presence or absence of trypsin in the chyme at the time of injury and with the serum level of intestinal hydrolases.

In the control group, the serum acid phosphatase ($P<0.05$, Table III) rises significantly one hour after the clamp is removed. In the hours after ischemia, the maximum rise in RNAase is also significantly higher ($P<0.05$). Comparison of these data with those in Group 2 (Table IV) shows that, in the treated group, the corresponding rise in acid phosphatase is not significant and there is no significant change in RNAase. These enzymes may originate from the lysed epithelial cells, lymphocytes, red cells and macrophages in the lamina propria. These elements are released into the blood during profound hemodynamic changes. As did Williams *et al.*,[53] we found that, in the control dogs (Table V), cardiac output dropped significantly even before declamping ($P<0.001$); there was a further drop one hour after declamping. These changes are accompanied by a fall in central venous pressure (CVP) left ventricular end-diastolic pressure (LVEDP) and blood pressure suggesting that blood is being pooled in the capacitance vessels, thus leading to a decreased cardiac output. These findings agree with other related observations in the course of shock. Direct studies of CVP[73-78] suggest that a drop in venous tone plays a role in various forms of refractory hypotension. It has been demonstrated experimentally that, at least in the early stages of irreversible shock,[79] peripheral vasculature makes a contribution that is distinct from cardiac failure. In shock, blood stagnates in the venules[80] and significant histological changes are seen in the vascular wall.[81] When venous tone is lost and the thin venous wall becomes distended, a large reservoir is created that may be a primary cause of the hemodynamic disturbance.[82] In the later stage of normovolemic shock, changes in peripheral vasculature do not appear to depend on neurogenic influences.[82-85] This lack of response and the apparent absence of beta receptors in the venous wall[85] strengthen the possibility that toxins have a role in the pathogenesis of vascular alterations. The rise in serum acid phosphatase in Group 1 is similar to that previously observed after two hours of hemorrhagic hypotension.[86] In treated dogs (Group 2) the rise in serum acid phosphatase is far less, while the average elevation in serum RNAase is almost nil. These basic differences suggest that, in Group 2, the cellular elements are preserved in the lamina propria (Table II). These two kinds of evidence suggest that the hydrolytic

TABLE VI.—Hemodynamic Data in Group 2 (Trypsin Inhibitor)

Dog no.	A Control values				B End of occlussion				Hours after release C 1 hour				D 48 hours			
	CO	BP	CVP	LVEDP	CO	BP	CVP	LVEDP	CO	BP	CVP	LVEDP	CO	BP	CVP	LVEDP
7598	125	120	0	0	110	125	+0.5	−6	110	130	+0.5	0	160	130	0	0
7610	132	150	0	0	132	125	+1	2	120	125	+1	2	133	100	+0.5	0
7621	100	140	0	0	78	125	+0.5	0	90	120	0	−1	—	—	+0.5	0
7634	160	125	0	0	156	118	−1	−2	147	100	0	−7	—	—	—	—
7639	157	120	0	0	152	125	+0.5	0	101	120	+0.5	0	—	—	—	—
7649	135	130	0	0	133	135	0	5	120	100	−0.5	−2	—	—	—	—
7651	160	150	0	0	80	125	−1	−7	60	125	−1	−7	—	125	0	—
7657	153	140	0	0	140	140	0	−1	154	130	0	0	180	135	—	0
7661	145	135	0	0	110	125	0	−2	90	100	−1	0	—	—	—	—
7681	94	135	0	0	100	135	0	−1	105	95	+0.5	+1	92	115	—	0
7701	183	140	0	0	183	130	0	0	160	100	0	0	225	100	+1.5	0
7712	128	95	0	—	130	110	0	—	110	90	−0.5	—	120	80	0	—
7693	150	100	0	0	125	115	−1	−5	80	100	−1	−5	—	—	—	—
Mean	140	129			125	125			111	110			152	112		
SEM	±6.89	±4.73			±8.29	±2.29			±8.12	±4.66			±19.29	±7.46		
Number	(13)	(13)			(13)	(13)			(13)	(13)			(6)	(7)		

CO A vs B $p < 0.3$ A vs C $p < 0.05$

CO = cardiac output (c.c./kg./min.); BP = mean arterial blood pressure (mm. Hg); CVP = central venous pressure (cm.H_2O) LVEDP = left ventricular end-diastolic pressure (mm. Hg).

enzymes found in the sera of the control dogs after ischemia originate primarily from the lamina propria, while most of the enzymes from the epithelial lining pass into the lumen and increase the enzymatic activity of chyme in both groups of dogs. As did Tice and Worth,[87] we found in *in vitro* studies that the trypsin inhibitor does not depress the activity of the hydrolytic cytoplasmic enzymes analyzed in the present study. Tice and Worth found that the rise of serum beta-glucuronidase after extracorporeal circulation could be prevented by administering a protease inhibitor; this inhibitor was thought to prevent the proteolytic release of intracellular lysosomal enzymes. It is equally significant that (concomitant with, and probably related to, the smaller increase in the serum level of intestinal enzymes) the hemodynamic effects of superior mesenteric artery occlusion are less significant in Group 2 (treated dogs, Table VI): the fall in cardiac output observed just before declamping is not significant but, one hour after declamping, the difference from the control values is significant ($P<0.05$). Thus, after acute intestinal ischemia, hydrolytic enzymes of intestinal origin are released into the systemic circulation at a time when profound hemodynamic changes are developing—a coincidence that may indicate a causal relationship. The severe hemolysis seen after intestinal ischemia (Table III) may reflect lysosomal action on the erythrocytes.[88, 89] Hemolysis in the controls (Group 1) was significant ($P< 0.005$), but not in the treated group (Table IV). Particularly interesting is the potential effect that free ribonuclease may have on vascular or cellular structures. Ledoux, Baltus and Vanderhaeghe[90] showed that RNAase penetrates ascites tumour cells and induces, at first, synthesis of abnormal RNA and then a decrease in RNA as the cell breaks down. Equally pertinent, Brachet[91] found that very low concentrations of ribonuclease (0.05 to 0.01 mg./ml.) produce cytolysis of amebae after only two to three hours. Because the RNAase rapidly penetrates the cell by pinocytosis, the cellular RNA rapidly declines. In *in vitro* studies, Deborin *et al.*[92] recently showed that RNAase exerts its lytic action across lipid membranes.

Although we do not suggest that the two specific hydrolases we examined cause the systemic vascular deterioration seen in intestinal ischemic shock, we would like to direct attention to De Duve's general thesis; namely, that all lysosomal hydrolases are released more or less together during non-selective disruption of lysosomal particles. Thus, if, after intracellular liberation of esterases (acid phosphatase) and nucleases (ribonuclease), these enzymes diffuse widely in the blood stream, lysosomal rupture may be linked to the development of irreversible hemodynamic changes.

SUMMARY

In the dog, temporary (two-hour) clamping of the superior mesenteric artery produces histological changes in the mucosa of the ileum similar to those observed in hemorrhagic shock.

When the clamp is released, the animals exhibit a decreased cardiac output, central venous pressure and arterial blood pressure; these evidences of hemodynamic deterioration after declamping indicate that blood has stagnated in the veins. The changes simulate the initial stages of shock.

Serum levels of acid phosphatase and RNAase from the lysed mucosal cells significantly increased.

The evolution of the mucosal necrosis and the subsequent hemodynamic and serum changes are worsened by the action of pancreatic proteolytic enzymes present in the chyme. Trypsin is particularly effective on the cellular and vascular elements of the lamina propria.

After ischemia some important changes take place in the chemical composition of the chyme: a marked decrease in free tryptic activity coincides with a simultaneous rise of free acid phosphatases and beta-glucuronidases from the ischemic mucosal cells.

The constant reflux of chyme, into the stomach, that has an altered enzymatic activity may link the intestinal lesion and the gastric stress ulcers seen in most of the dogs that survived intestinal ischemic shock.

The author wishes to express his appreciation to Dr. R. F. P. Cronin for advice and consultation and to Miss Louise Carpentier, R.T., for technical assistance.

REFERENCES

1. DUPUYTREN, G.: Clinical lectures on surgery, chapter 16, translation of Leçons orales de clinique chirurgicale 1832, Collins & Hannay, New York, 1833.
2. CUMIN, W.: Cases of severe burn with dissections and remarks, *Edinburgh Medical and Surgical Journal*, **19:** 337, 1823.
3. SWAN, J.: Case of a severe burn, *Edinburgh Medical and Surgical Journal*, **19:** 344, 1823.
4. CURLING, T. B.: On acute ulceration of the duodenum in cases of burn, *Med.-Chir. Trans.*, **25:** 260, 1842.
5. BILLROTH, T.: Ueber Duodenalgeschwüre bei Septicämie, *Wien. Med. Wschr.*, **17:** 705, 1867.
6. GRÉGOIRE, R.: Pathogénie des infarctus viscéreaux, *Mém. Acad. Chir. (Paris)*, **63:** 930, 1937.
7. PENNER, A. AND BERNHEIM, A. I.: Acute postoperative enterocolitis; study on the pathologic nature of shock, *Arch. Path. (Chicago)*, **27:** 966, 1939.
8. SILVER, P. G.: Fatal haemorrhage from a duodenal ulcer, associated with a toxic adenoma of the thyroid gland, *Canad. Med. Ass. J.*, **15:** 517, 1925.
9. HERBUT, P. A.: Acute peptic ulcers following distant operations, *Surg. Gynec. Obstet.*, **80:** 410, 1945.
10. WOLDMAN, E. E.: Acute ulcers of upper gastrointestinal tract; their relation to systemic stress and adrenal damage, *J.A.M.A.*, **149:** 984, 1952.
11. FREBERT, H.: Infarctus iléal sans lésion vasculaire, *Mém. Acad. Chir. (Paris)*, **78:** 661, 1952.
12. WILSON, R. AND QUALHEIM, R. E.: A form of acute hemorrhagic enterocolitis afflicting chronically ill individuals; description of twenty cases, *Gastroenterology*, **27:** 431, 1954.
13. LUNA, C. A. F. AND TINELLI, J. C.: Infarto intestinomesenterico inexplicado, *Prensa Med. Argent.*, **43:** 669, 1956.
14. BERKOWITZ, D., WAGNER, B. M. AND URICCHIO, J. F.: Acute peptic ulceration following cardiac surgery, *Ann. Intern. Med.*, **46:** 1015, 1957.
15. ENDE, N.: Infarction of the bowel in cardiac failure, *New Eng. J. Med.*, **258:** 879, 1958.
16. KATZ, A. M.: Hemorrhagic duodenitis in myocardial infarction, *Ann. Intern. Med.*, **51:** 212, 1959.
17. GLOTZER, D. J. AND SHAW, R. S.: Massive bowel infarction; an autopsy study assessing the potentialities of reconstructive vascular surgery, *New Eng. J. Med.*, **260:** 162, 1959.
18. MING, S.-C. AND LEVITAN, R.: Acute hemorrhagic necrosis of the gastrointestinal tract, *New Eng. J. Med.*, **263:** 59, 1960.
19. CARTER, R. D. AND ASHLEY, C. A.: A clinical and postmortem study of acute ulcerative esophagitis and enterocolitis, *Surg. Clin. N. Amer.*, **40:** 957, 1960.
20. HOFFMAN, F. G., ZIMMERMAN, S. L. AND CARDWELL, E. S.: Massive intestinal infarction without vascular occlusion associated with aortic insufficiency, *New Eng. J. Med.*, **263:** 436, 1960.
21. BLENNERHASSETT, J. B. AND REID, J. D.: Intestinal infarction: with particular reference to cases occurring without macroscopic occlusion of vessels, *New Zeal. Med. J.*, **59:** 131, 1960.
22. GAZES, P. C. *et al.*: Acute hemorrhage and necrosis of intestines associated with digitalization, *Circulation*, **23:** 358, 1961.
23. BERGER, R. L. AND BYRNE, J. J.: Intestinal gangrene associated with heart disease, *Surg. Gynec. Obstet.*, **112:** 529, 1961.
24. CORDAY, E. *et al.*: Mesenteric vascular insufficiency. Intestinal ischemia induced by remote circulatory disturbances, *Amer. J. Med.*, **33:** 365, 1962.
25. ROBERTSON, R. AND DODDS, W. A.: Mesenteric artery insufficiency complicating repair of

aortic regurgitation, *Canad. J. Surg.*, **7:** 269, 1964.
26. Drucker, W. R. *et al.*: Hemorrhagic necrosis of the intestine. A clinical syndrome: presence without organic vascular occlusion, *Arch. Surg. (Chicago)*, **89:** 42, 1964.
27. Heer, F. W., Silen, W. and French, S. W.: Intestinal gangrene without apparent vascular occlusion, *Amer. J. Surg.*, **110:** 231, 1965.
28. Herman, B. and Hermanova, K.: Haemorrhagische Komplikationen des Verdauungstraktes bei Herzkrankheiten, *Gastroenterologia (Basel)*, **104:** 352, 1965.
29. Kligerman, M. J. and Vidone, R. A.: Intestinal infarction in the absence of occlusive mesenteric vascular disease, *Amer. J. Cardiol.*, **16:** 562, 1965.
30. Grosh, J. L., Mann, R. H. and O'Donnell, W. M.: Nonthrombotic intestinal infarction in heart disease, *Amer. J. Med. Sci.*, **250:** 613, 1965.
31. Freiman, D. G.: Hemorrhagic necrosis of the gastrointestinal tract, *Circulation*, **32:** 329, 1965.
32. Bhagwat, A. G. and Hawk, W. A.: Terminal hemorrhagic necrotizing enteropathy (THNE). A retrospective clinicopathologic study with a review of literature, *Amer. J. Gastroent.*, **45:** 163, 1966.
33. Messmer, B., Middendorp, U. and Maranta, E.: Zum funktionell-spastischen Mesenterialinfarkt, *Helv. Chir. Acta*, **33:** 521, 1966.
34. Brawley, R. K., Roberts, W. C. and Morrow, A. G.: Intestinal infarction resulting from nonobstructive mesenteric arterial insufficiency, *Arch. Surg. (Chicago)*, **92:** 374, 1966.
35. Haller, J. D., Pena, C. and Dargan, E. L.: Massive upper-gastrointestinal hemorrhage due to pancreatitis, *Arch. Surg. (Chicago)*, **93:** 567, 1966.
36. Fogarty, T. J. and Fletcher, W. S.: Genesis of nonocclusive mesenteric ischemia, *Amer. J. Surg.*, **111:** 130, 1966.
37. Muggia, F. M.: Hemorrhagic necrosis of the intestine: its occurrence with digitalis intoxication, *Amer. J. Med. Sci.*, **253:** 263, 1967.
38. Williams, L. F. *et al.*: Non occlusive mesenteric infarction, *Amer. J. Surg.*, **114:** 376, 1967.
39. Carey, J. S. *et al.*: Intestinal infarction in shock with survival after resection; relation of the intestinal lesion to shock with high cardiac output, *J. A. M. A.*, **199:** 422, 1967.
40. Ottinger, L. W. and Austen, W. G.: Study of 136 patients with mesenteric infarction, *Surg. Gynec. Obstet.*, **124:** 251, 1967.
41. Ousterhout, D. K. and Feller, I.: Occult gastrointestinal hemorrhage in burned patients, *Arch. Surg. (Chicago)*, **96:** 420, 1968.
42. Bounous, G., Hampson, L. G. and Gurd, F. N.: Cellular nucleotides in hemorrhagic shock: relationship of intestinal metabolic changes to hemorrhagic enteritis and the barrier function of intestinal mucosa, *Ann. Surg.*, **160:** 650, 1964.
43. Bounous, G. *et al.*: Abolition of 'tryptic enteritis' in the shocked dog. Creation of an experimental model for study of human shock and its sequelae, *Arch. Surg. (Chicago)*, **91:** 371, 1965.
44. Bounous, G.: Metabolic changes in the intestinal mucosa during hemorrhagic shock, *Canad. J. Surg.*, **8:** 332, 1965.
45. Tiberio, G. *et al.*: Sur la prévention de l'entérite nécrotico-hémorragique provoquée par le choc hypovolémique irréversible expérimental, *Lyon Chir.*, **64:** 605, 1968.
46. Hiatt, N. *et al.*: Nitrogen mustard hyperamylasemia and intestinal lesions, *Surgery*, **61:** 596, 1967.
47. Hiatt, N. and Warner, N. E.: Influence of intestinal content on radiation lesions of the small intestine, *Proc. Soc. Exp. Biol. Med.*, **124:** 937, 1967.
48. Morgenstern, L. and Hiatt, N.: Injurious effect of pancreatic secretions on post-radiation enteropathy, *Gastroenterology*, **53:** 923, 1967.
49. Smith, E. E. *et al.*: Intestinal fluid loss in dogs during irreversible hemorrhagic shock, *Surg. Gynec. Obstet.*, **125:** 45, 1967.
50. Laufman, H.: In discussion: Evans, W. E. *et al.*: Effect of intestinal exclusion in *Escherichia coli* endotoxin shock, *Arch. Surg. (Chicago)*, **95:** 516, 1967.
51. Black-Schaffer, B. *et al.*: The pathogenesis of the intestinal lesion of deep hypothermia and a proposed relationship to that of irreversible shock, including a note on a mechanism for the normal turnover of intestinal epithelium, *Surgery*, **61:** 904, 1967.
52. Bounous, G.: Role of the intestinal contents in the pathophysiology of acute intestinal ischemia, *Amer. J. Surg.*, **114:** 368, 1967.
53. Williams, L. F. *et al.*: Experimental nonocclusive mesenteric ischemia, *Amer. J. Surg.*, **115:** 82, 1968.
54. Lillehei, R. C.: The intestinal factor in irreversible hemorrhagic shock, *Surgery*, **42:** 1043, 1957.
55. Ankeney, J. L., Coffin, L. H. and Littel, A. S.: Experimental evidence that vasoconstriction in hemorrhagic shock does not result in anaerobic metabolism, *Ann. Surg.*, **166:** 365, 1967.
56. Bashour, F. A., Nafrawi, A. G. and McClelland, R. N.: Splanchnic hemodynamics and carbohydrate metabolism in hemorrhagic shock. *In*: Shock and hypotension; pathogenesis and treatment. The twelfth Hahnemann symposium, edited by L. C. Mills and J. H. Moyer, Grune & Stratton Inc., New York, 1965, p. 265.
57. Hamrick, L. W., Jr. and Myers, J. D.: The effect of hemorrhage on hepatic blood flow and splanchnic oxygen consumption of the dog, *Circ. Res.*, **3:** 65, 1955.
58. Bounous, G., Hampson, L. G. and Gurd, F. N.: Regional blood flow and oxygen consumption in experimental hemorrhagic shock, *Arch. Surg. (Chicago)*, **87:** 340, 1963.
59. Bounous, G. *et al.*: The prophylactic use of an 'elemental' diet in experimental hemorrhagic shock and intestinal ischemia, *Ann. Surg.*, **166:** 312, 1967.
60. Selkurt, E. E.: Role of liver and toxic factors in shock. *In*: Shock, edited by S. G. Hershey, Little, Brown & Co. Inc., Boston, 1964, p. 43.
61. Palmerio, C. *et al.*: Denervation of the abdominal viscera for the treatment of traumatic shock, *New Eng. J. Med.*, **269:** 709, 1963.

62. Evans, W. E. *et al.*: Effect of intestinal exclusion in *Escherichia coli* endotoxin shock, *Arch. Surg. (Chicago)*, **95:** 511, 1967.
63. Beau, A. F.: A method for hemoglobin in serum and urine, *Amer. J. Clin. Path.*, **38:** 111, 1962.
64. Sigma Chemical Co.: Acid phosphatase assay, Technical bulletin 104, New York, 1963.
65. Sigma Chemical Co.: Serum lipase, Technical bulletin 800, St. Louis, 1967.
66. Sigma Chemical Co.: Amylase in serum, urine or other fluids, Technical bulletin 700, St. Louis, 1965.
67. Fishman, W. H., Springer, B. and Brunetti, R.: Application of an improved glucuronidase assay method to the study of human blood β-glucuronidase, *J. Biol. Chem.*, **173:** 449, 1948.
68. Lundh, G.: Determination of trypsin and chymotrypsin in human intestinal content, *Scand. J. Clin. Lab. Invest.*, **9:** 229, 1957.
69. Kiekens, R.: Digestion et absorption digestive des graisses et des protéines chez le sujet normal et après gastrectomie, Acta Medica Belgica, Bruxelles, 1963.
70. Bounous, G. and McArdle, A. H.: Release of intestinal enzymes in acute mesenteric ischemia, *J. Surg. Res.*, **9:** 339, 1969.
71. Scott, J. B. and Dabney, J. M.: Relation of gut motility to blood flow in the ileum of the dog, *Circ. Res.*, **15** (Suppl. 1)**:** 234, 1964.
72. Goldberg, D. M., McAllister, R. A. and Roy, A. D.: Studies on human intestinal proteolysis, *Scand. J. Gastroent.*, **3:** 193, 1968.
73. Andersen, D. and Klebe, J. G.: Measurement of central venous pressure; its use in the transfusion treatment of patients with gastroduodenal haemorrhage, *Scand. J. Gastroent.*, **3:** 113, 1968.
74. Cournand, A. *et al.*: Studies of the circulation in clinical shock, *Surgery*, **13:** 964, 1943.
75. MacLean, L. D.: The clinical management of shock, *Brit. J. Anaesth.*, **38:** 255, 1966.
76. Fell, C.: Changes in distribution of blood flow in irreversible hemorrhagic shock, *Amer. J. Physiol.*, **210:** 863, 1966.
77. Rothe, C. F. and Selkurt, E. E.: Cardiac and peripheral failure in hemorrhagic shock in the dog, *Amer. J. Physiol.*, **207:** 203, 1964.
78. Alexander, R. S.: Venomotor tone in hemorrhage and shock, *Circ. Res.*, **3:** 181, 1955.
79. Rothe, C. F., Love, J. R. and Selkurt, E. E.: Control of total vascular resistance in hemorrhagic shock in the dog, *Circ. Res.*, **12:** 667, 1963.
80. Bor, N. M. *et al.*: Capillary circulation; characteristics during treatment of shock by means of artificial heart-lung procedures in the dog, *J. A. M. A.*, **179:** 417, 1962.
81. Ashford, T., Palmerio, C. and Fine, J.: Structural analogue in vascular muscle to the functional disorder in refractory traumatic shock and reversal by corticosteroid; electron microscopic evaluation, *Ann. Surg.*, **164:** 575, 1966.
82. Landis, E. M. and Hortenstine, J. C.: Functional significance of venous blood pressure, *Physiol. Rev.*, **30:** 1, 1950.
83. Bond, R. F., Manley, E. S., Jr. and Green, H. D.: Cutaneous and skeletal muscle vascular responses to hemorrhage and irreversible shock, *Amer. J. Physiol.*, **212:** 488, 1967.
84. Rothe, C. F., Schwendenmann, F. C. and Selkurt, E. E.: Neurogenic control of the skeletal muscle vascular resistance in hemorrhagic shock, *Amer. J. Physiol.*, **204:** 925, 1963.
85. Wood, J. E.: The venous system, *Sci. Amer.*, **218:** 86, January 1968.
86. Sutherland, N. G., Bounous, G. and Gurd, F. N.: Role of intestinal mucosal lysosomal enzymes in the pathogenesis of shock, *J. Trauma*, **8:** 350, 1968.
87. Tice, D. A. and Worth, M. H.: Cellular damage associated with extracorporeal perfusion: plasminogen activation and lysosomal enzyme activity, *Surgery*, **63:** 669, 1968.
88. Seaman, G. V., Jackson, L. J. and Uhlenbruck, G.: Action of α-amylase preparations and some proteases on the surface of mammalian erythrocytes, *Arch. Biochem.* **122:** 605, 1967.
89. Desai, I. D. and Tappel, A. L.: Erythrocyte hemolysis by isolated rat liver lysosomes, *Proc. Soc. Exp. Biol. Med.*, **118:** 496, 1965.
90. Ledoux, L., Baltus, E. and Vanderhaeghe, F.: Effet de la ribonucléase sur l'incorporation de l'adénine et de la phénylalanine dans les cellules d'ascites 'in vitro', *Arch. Int. Physiol.*, **64:** 135, 1956 (extract).
91. Brachet, J.: Biochemical cytology, Academic Press Inc., New York, 1957, p. 268.
92. Deborin, G. A. *et al.*: Enzymatic breakdown of ribonucleic acid separated from ribonuclease by a lipid membrane, *Fed. Proc.* [*Trans. Suppl.*], **25:** 863, 1966.

Résumé

Pour pouvoir étudier le facteur intestinal dans le choc, l'auteur a produit un choc expérimental chez le chien par occlusion temporaire de l'artère mésentérique supérieure. Cette méthode a provoqué dans la muqueuse intestinale des modifications anatomiques semblables à celles qu'on observe au cours du choc hémorragique chez l'homme. La libération concomitante dans le sang de phosphatase acide et de RNAase et la chute du débit cardiaque et de la tension artérielle témoignent clairement qu'on est en présence d'un intestin ischémique. Dans le chyme, après l'ischémie, une nette diminution de l'activité de la trypsine libre survient en même temps que l'augmentation simultanée de la phosphatase acide et de bêta-glucuronidase des cellules ischémiées de la muqueuse. La régurgitation gastrique constante du chyme dont l'activité enzymatique est altérée peut constituer le lien pathogène entre la lésion intestinale et les ulcères gastriques par stress qu'on note chez la majorité des chiens qui ont survécu au choc ischémique intestinal. L'évolution vers la nécrose de la muqueuse ischémique et les modifications subséquentes dans l'hémodynamique et les enzymes sériques sont aggravées par l'action digestive des enzymes protéolytiques du pancréas qui sont présentes dans le chyme. La trypsine est particulièrement active sur les éléments cellulaires et vasculaires de la lamina propria. L'inhibition préalable de la trypsine dans le chyme permet de réduire les effets gastriques et généraux de l'entéropathie ischémique.

POSTOPERATIVE GASTRIC MOTILITY*

B. D. FEAVER, M.D., J. S. CRISPIN, M.D., F.R.C.S.[C] and
J. F. LIND, M.D., F.R.C.S.[C], F.A.C.S., *Winnipeg, Man.*

In the immediate postoperative period, gastric motility ceases clinically and returns in 48 to 72 hours. Very little understanding of the pathophysiology of this phenomenon has been acquired.

In 1961 Baker and Dudley[1] studied patients after operation by auscultation and by means of radiographs taken at eight-hour intervals. They concluded that some form of intestinal transport persisted after operation, but were unable to say if this was gastric, intestinal, or both. By auscultation, they concluded that a silent abdomen indicated abnormality and that the passage of gas per rectum may be delayed; hence, it was not a useful sign in assessing intestinal motility.

In 1963 Rothnie, Harper and Catchpole[2] studied 31 patients postoperatively by radiological methods. Eight of these had upper abdominal surgery not involving the stomach. Contrast medium was introduced into the stomach immediately after operation and films were taken at the time of introduction, 18, 24 and 48 hours after operation. These investigators found that the stomach was inactive for 18 to 24 hours, but that the small intestine was capable of motility and propulsion. They concluded that the early postoperative abdomen was silent because of the lack of intestinal content. Wells *et al.*[3] came to similar conclusions after using auscultation and kymography in 10 patients.

In 1964 Goodall,[4] using intraluminal balloon manometry, studied the motility of the stomach and duodenum in 10 patients after cholecystectomy. He subdivided the types of pressure waves according to the methods presently used in gastroenterology[5] and also recorded times of reappearance of the various pressure waves. He showed that gastric activity ceased after operation and returned in an average of 10 hours. Duodenal activity, however, had returned in all patients in an average of five hours after operation.

In the present investigation, we studied gastric motility by means of intraluminal manometry using the open-tipped tube. This technique has been developed in recent years to circumvent some of the difficulties inherent in pressure recording using balloon manometry.

Method

Nine patients (six women and three men) were chosen at random from those undergoing cholecystectomy. They ranged in age from 21 to 68 years, with a mean age of 51. The apparatus and technique of recording used were described previously by Lind, Blanchard and Guyda.[6] Their method was modified slightly: the three open-tipped tubes were attached to the tip of a radiopaque Levin tube and fixed by silk ligature (Fig. 1). The tubes had lateral orifices at intervals of 5 cm. measured from the tip of the radiopaque

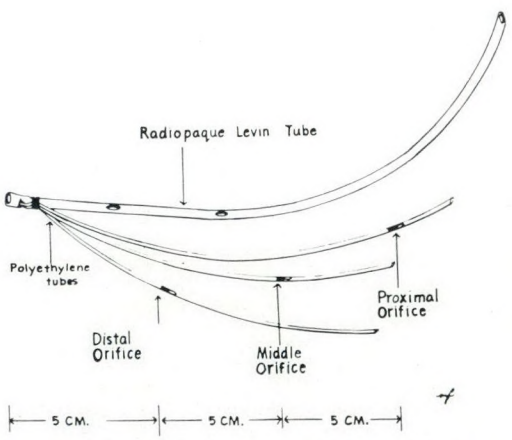

Fig. 1.—Pressure detecting units attached to a nasogastric tube.

*From the Departments of Radiology and Surgery, University of Manitoba, and the Gastroenterology Unit, Winnipeg General Hospital, Winnipeg, Man.

Supported in part by a grant from the Medical Research Council of Canada.

Presented at the Annual Meeting of the Royal College of Physicians and Surgeons of Canada, Vancouver, B.C., January 1969.

Reprint address: Dr. J. F. Lind, Department of Surgery, Winnipeg General Hospital, Winnipeg 3, Man.

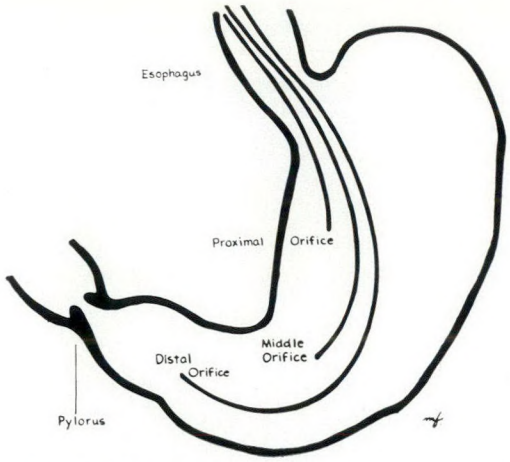

Fig. 2.—The position of pressure detecting units within the stomach.

tube. During recording, saline was infused constantly through the three open-tipped tubes.

The study began before operation. The recording tubes were passed through the nose into the stomach and positioned fluoroscopically with the tip of the radiopaque tube in the terminal antrum. The position of the orifices is illustrated in Fig. 2. The first recording was made as soon after admission as was practical. Each recording was continued for 60 minutes. In addition, in three patients, a record was obtained after the patient received a preoperative sedative consisting of meperidine (Demerol) 50 mg. and atropine 0.6 mg.

After operation the position of the recording tubes was confirmed radiologically (Fig. 3). Then the recording was continued for one hour and, thereafter, at intervals of four hours except between 12:00 midnight and 7:00 a.m. On individual patients recordings were made up to 60 hours after operation.

Intestinal tract pressure wave types have been classified as follows:[5, 7] Type I waves—simple monophasic waves of up to 10 cm. H_2O pressure lasting up to 20 seconds; Type II waves—monophasic, with amplitudes greater than 10 cm.H_2O and lasting from 12 to 60 seconds; Type III waves—complex, consisting of an increase in baseline pressure upon which Type I or Type II waves were superimposed. Fig. 4 shows a typical pressure recording.

In interpreting the motility records, we determined the duration of each pressure wave by measuring the distance between the points where the pressure tracing left and returned to the baseline. The total activity was expressed as a percentage of the total recording time in seconds. The same method was applied to each specific wave type but the totals were expressed as percentages of mean total gastric activity. Similarly, the amplitude of each contraction was calculated by measuring the distance from the baseline to the wave peak and was expressed in centimetres of saline. After the initial analysis of data obtained in each patient, the total data were further analyzed by arbitrarily dividing the recording time into periods of five hours. Zero time was designated as the conclusion of the operation. Each five-hour period included recordings made 2½ hours before and after the time period indicated.

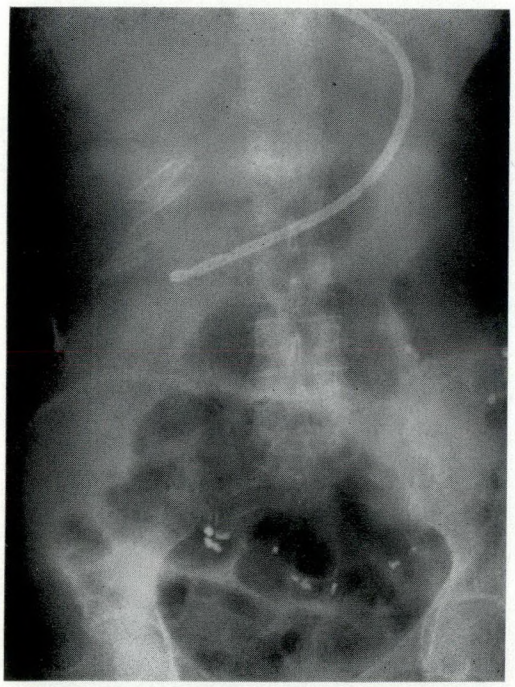

Fig. 3.—Postoperative radiograph of the nasogastric tube and attached pressure detecting units positioned within the stomach.

Results

Gastric activity was recorded in all patients before operation. Peristalsis was also

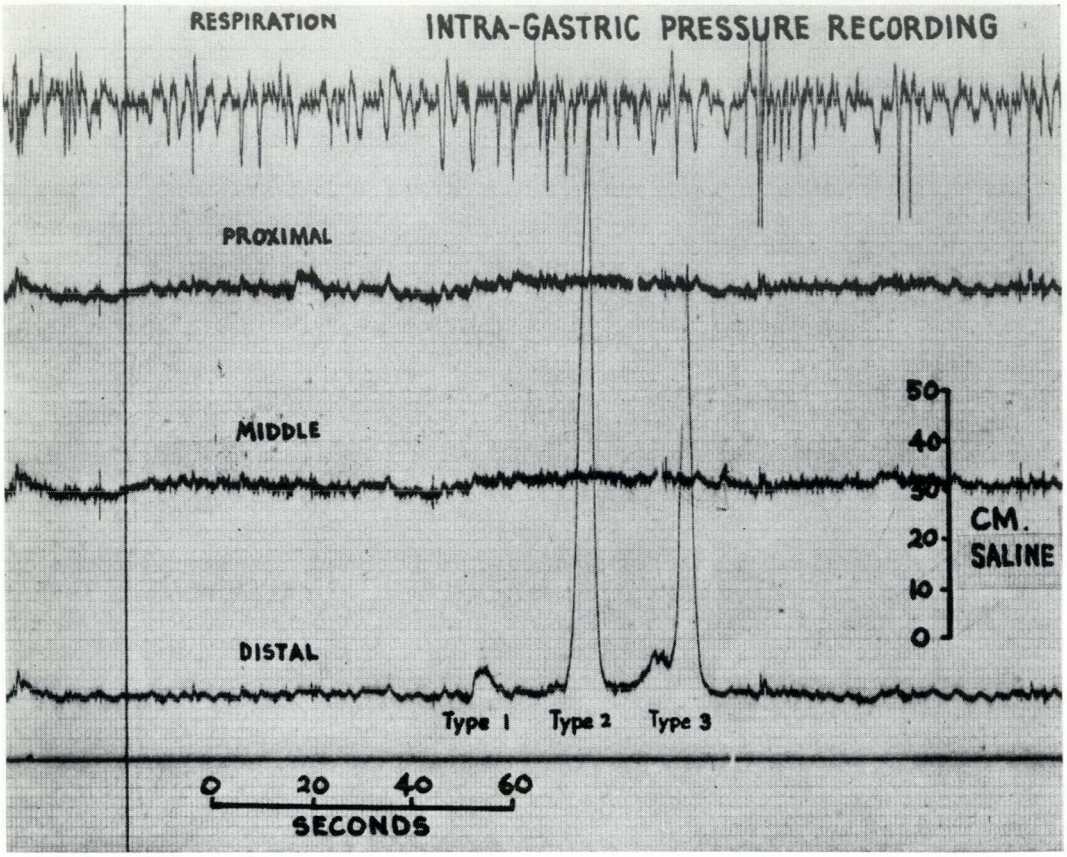

Fig. 4.—Intragastric pressure wave types, recorded by three open-tipped tubes (proximal, middle and distal). The upper tracing is a recording of respiration (inspiratory deflection downward).

recorded in each patient during this period. In three patients on whom recordings were made after premedication, gastric activity slowed and then ceased within 15 minutes of the injection of the drugs.

The study of the data obtained in individual patients revealed that detectable gastric activity was absent immediately after cholecystectomy. The duration of inactivity varied from 5 to 20 hours. In five patients, Type I activity was the first to appear, followed by Types II and III in no specific sequence. In eight of the nine patients, gastric activity had returned to 85% or more of the preoperative level by 50 hours, and in the ninth patient had returned to 40% in 50 hours.

Using this data from all patients, mean values for gastric activity were calculated for each five-hour period. The mean total preoperative activity was 31.1% of the total recording time. Of this total, 9.6% was Type I, 7.1% was Type II, and 14.4% was Type III activity. For ease of interpretation, all other values were expressed as a percentage of the mean total gastric activity.

Accordingly, total preoperative activity declined from 100% to zero at operation

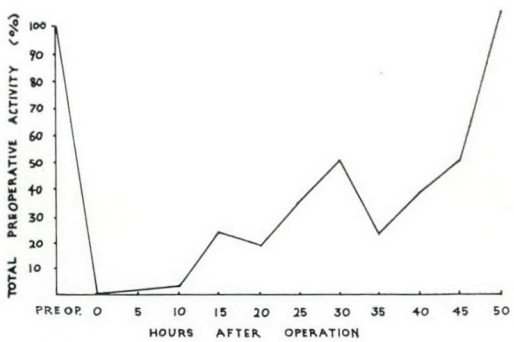

Fig. 5.—Total gastric activity expressed as a percentage of total preoperative activity (nine patients).

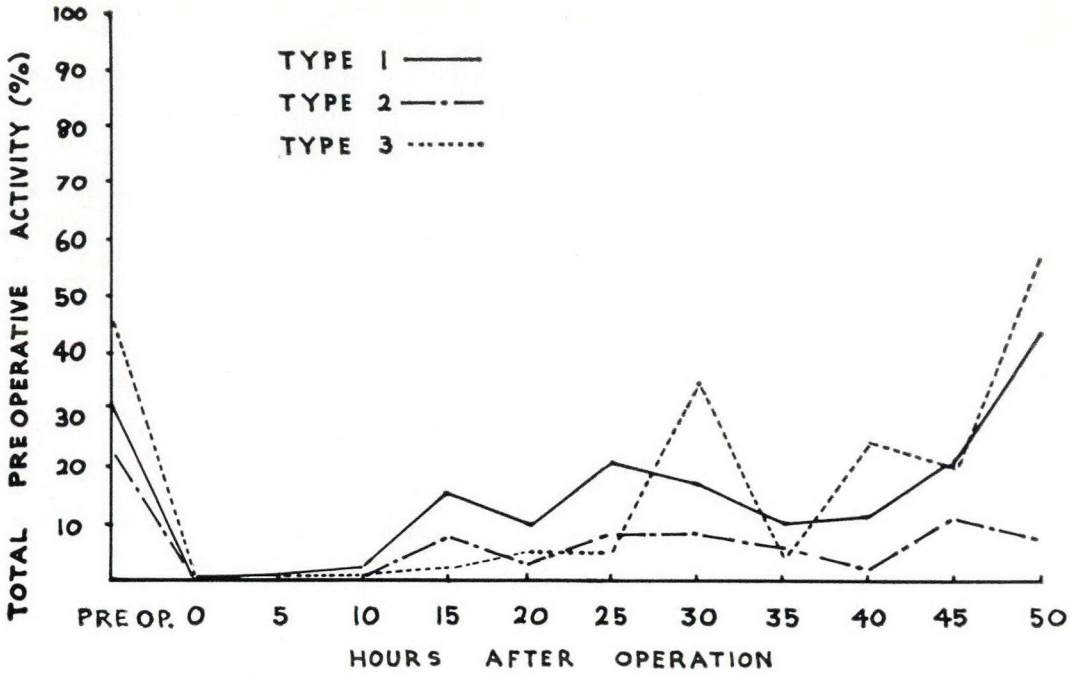

Fig. 6.—Types of gastric motor activity in preoperative and postoperative phases expressed as a percentage of total preoperative activity (nine patients).

and remained at less than 1.5% for 10 to 12 hours. Between 10 and 35 hours total activity gradually increased with fluctuations, followed by an abrupt rise between 35 and 50 hours to a level of 103% at 50 hours (Fig. 5). During this latter period, peristaltic waves were first seen.

Type I activity, 30.9% before operation, was less than 1.5% immediately after operation and remained at this level for 10 to 12 hours. Between 10 and 35 hours it gradually increased with fluctuations, and between 35 and 50 hours rose abruptly to a level of 41.1%. Type III activity showed a similar pattern, declining from a preoperative level of 46.3% to complete cessation at operation where it remained for 10 to 12 hours. After a gradual reappearance with fluctuations there was an abrupt rise in activity between 35 and 50 hours. By 50 hours Type III activity had returned to 56.5%. Type II activity on the other hand declined from a preoperative level of 23% to zero at operation and by 50 hours had returned to only 5.9% (Fig. 6).

Discussion

In this study we attempted to relate the period of gastric inactivity to the type of preoperative medication, type and length of anesthesia, incision and operative procedure. We were unable to demonstrate any consistent relationship between gastric activity and any of these variables. Similarly, there was no increase or decrease in gastric activity after the patient received postoperative analgesia. It is likely that the degree of inactivity depends upon reflex or direct inhibition of the stomach due to manipulation at operation.

No specific pattern of recurrence of each wave type was recognized. However, some similarities were apparent. Activity in all patients reappeared slowly and then remained at a low level for 30 hours. Considerable fluctuation in levels of activity was seen in each patient, with periods of relatively greater activity followed by periods of relatively less activity. After these fluctuations the level of activity was always greater than that which preceded the fluctuations. During the period 30 to 50 hours

after operation, abrupt increases in activity were recorded without the fluctuations of the earlier periods. Peristaltic activity was first recorded during this interval. Activity steadily returned to the preoperative levels.

During each recording session the presence or absence of bowel sounds was noted. Bowel sounds were audible in all patients before operation, while after operation bowel sounds were clearly audible before any significant level of gastric activity was recorded.

The disappearance and gradual return of gastric motility in patients undergoing cholecystectomy correlate well with what is observed clinically in such patients. Although there is considerable individual variation as to quantity of activity and the time required for activity to return to preoperative levels, all patients showed the same general pattern.

Summary

Postoperative gastric motility was investigated in nine patients who had undergone cholecystectomy. Changes in intragastric pressure were recorded through open-tipped tubes.

Gastric motility was present in all patients before operation, and in three patients it ceased within 15 minutes of administration of the preoperative medication. Gastric motility was absent in all patients for 5 to 20 hours after operation. In eight of the nine patients total gastric activity returned to 85% or more of the preoperative level within 35 to 50 hours after operation. In five patients Type I activity was the first to return. There was no specific pattern of reappearance in the remaining four patients. All types of gastric activity reappeared slowly until 35 hours after operation. At this time, Types I and III showed an abrupt increase in activity up to 50 hours. A similar increase in Type II activity was not recorded during the latter period.

The authors wish to thank Drs. T. K. Thorlakson and C. W. Clark, Mrs. Donna Meade, R.N., Mrs. Sharon Trosky, R.N., Miss K. Doern, R.N. and Mrs. B. Bonner, R.N. Mrs. Margaret Feaver graciously provided the illustrations.

References

1. Baker, L. W. and Dudley, H. A. F.: Auscultation of the abdomen in surgical patients, *Lancet*, **2:** 517, 1961.
2. Rothnie, N. G., Harper, R. A. K. and Catchpole, B. N.: Early postoperative gastrointestinal activity, *Lancet*, **2:** 64, 1963.
3. Wells, C. *et al.*: Postoperative gastrointestinal motility, *Lancet*, **1:** 4, 1964.
4. Goodall, P.: Early gastroduodenal motility following operation, *Brit. J. Surg.*, **51:** 864, 1964.
5. Hightower, N. C. and Code, C. F.: The quantitative analysis of antral gastric motility records in normal human beings, with a study of the effects of neostigmine, *Proc. Mayo Clin.*, **25:** 697, 1950.
6. Lind, J. F., Blanchard, R. J. and Guyda, H.: Esophageal motility in tracheoesophageal fistula and esophageal atresia, *Surg. Gynec. Obstet.*, **123:** 557, 1966.
7. Lorber, S. H. and Shay, H.: Technical and physiological considerations in measuring gastrointestinal pressures in man, *Gastroenterology*, **27:** 478, 1954.

Résumé

Les auteurs ont étudié la motilité gastrique post-opératoire chez neuf malades qui avaient subi une cholécystectomie. Les changements de la pression intragastrique ont été enregistrés par un tube à bout ouvert.

Avant l'opération, la motilité gastrique existait chez tous les patients. Chez trois d'entre eux, elle cessa 15 minutes après l'administration de la médication pré-opératoire. Chez tous les opérés, la motilité gastrique a été absente durant une période de 5 à 20 heures. Chez huit des neuf opérés, l'activité gastrique globale revient à au moins 85% de son niveau pré-opératoire dans un délai de 35 à 50 heures. Chez cinq patients, une activité gastrique du type I fut la première à réapparaître. Chez les quatre autres, on ne put discerner un ordre précis de réapparition de la motilité. Tous les types d'activité gastrique refirent lentement leur apparition dans les 35 heures suivant l'opération. A cette période, l'activité des types I et III reprit brusquement jusqu'à 50 heures. On n'a pu noter une semblable augmentation de l'activité du type II pendant cette dernière période.

LEIOMYOSARCOMA ARISING FROM VEINS: TWO CASES AND A REVIEW OF THE LITERATURE ON VENOUS NEOPLASMS*

I. J. SZASZ, M.D., R. BARR, M.B., Ch.B., C.R.C.P.[C] and
T. K. SCOBIE, M.D., M.Sc., F.R.C.S.[C], F.A.C.S.,
Ottawa, Ont.

IN this paper we wish to present two patients with leiomyosarcoma arising from veins who were treated recently at the Ottawa Civic Hospital. Because such tumours are rare, we have reviewed the medical literature and presented our findings.

CASE REPORTS

Case 1.—T.S., a 68-year-old man, was admitted to the Ottawa Civic Hospital in September 1961 because of mild, congestive cardiac failure. On examination he had a mass measuring approximately 2.5 x 5 cm. on the anteromedial aspect of the middle third of his thigh. This was fixed to underlying tissues but not to the skin and was not painful or tender. He had no palpable lymph nodes. At operation the lesion, which involved the long saphenous vein but was not fixed to neighbouring tissues, was excised with an adequate portion of the vein.

The specimen submitted for pathological examination, which measured 5.5 x 4 x 3 cm., consisted of a roughly oval tumour. A vein protruded from one end and a cylindrical projection from the other (Fig. 1). The outer surface was grey and ragged. On cross-section a uniform, white, fleshy mass surrounded the vein, involving its wall, and finger-like extensions projected into the lumen. On microscopy the specimen was composed of fascicles and whorls of spindle-shaped cells (Fig. 2). The nuclei were vesicular and there was a moderate number of mitotic figures. The diagnosis was leiomyosarcoma, most likely arising from the long saphenous vein.

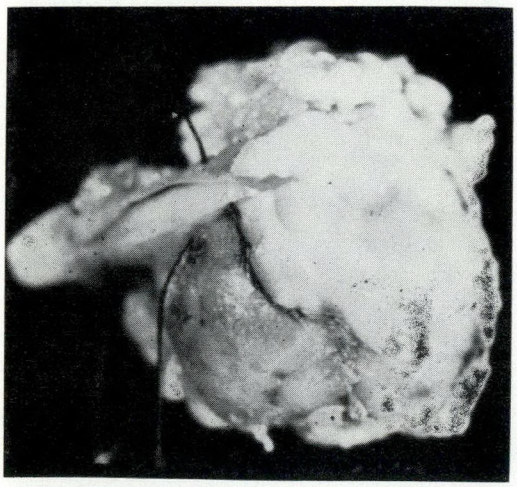

Fig. 1.—Case 1. The tumour surrounds the vein from which it arose. The vein can be identified by the silk suture around it.

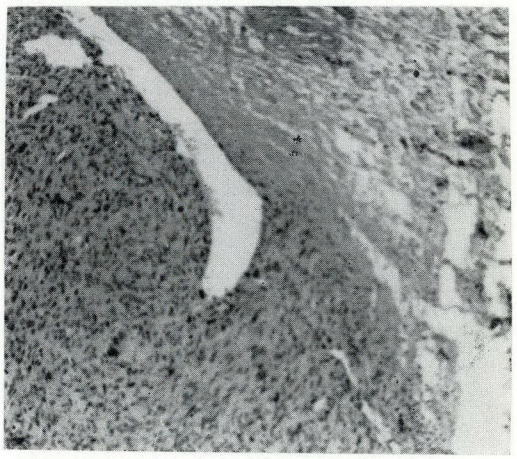

Fig. 2.—Case 1. Photomicrograph showing the wall of the saphenous vein and the origin of the tumour (original magnification x 200).

The patient made an uneventful recovery and was well until October 1963, when he was readmitted, complaining of pain associated with a pedunculated mass on his left cheek. This mass, which measured approximately 3.5 x 1.5 cm., was widely excised and found to be leiomyosarcoma. Nine months later this same tumour recurred and was once more excised. At the same time, we found a small mass in his left groin. He was readmitted again in December 1964 with marked hepatomegaly. Radioactive liver scan and open-liver biopsy confirmed the clinical diagnosis of secondary leiomyosarcoma. He died of liver failure in October 1965.

Case 2.—H.H., a 37-year-old man, was first seen in January 1967 because he had a gradu-

*From the Departments of Surgery and Pathology, Ottawa Civic Hospital, and the University of Ottawa Medical School, Ottawa, Ont.

ally increasing, asymptomatic mass on the right side of his neck which had been present for about nine months. This mass, which measured approximately 5 x 6 cm., was not fixed to the skin. Transmitted pulsation could be felt, but no bruit was heard. We biopsied the mass under general anesthesia but, because of its location and our doubt concerning the true diagnosis at that time, we did not excise the tumour. Paraffin-embedded sections of the tumour showed leiomyosarcoma. The patient was referred to the vascular surgery service. Carotid and vertebral angiograms were normal. His neck was explored and a right radical dissection performed. At the time of operation the tumour appeared to arise from the internal jugular vein, between the common facial and superior thyroid veins, distorting both structures. There were numerous distended collateral veins. The carotid vessels appeared to be free of involvement.

The specimen submitted for pathological examination measured 9 x 3 x 5 cm. Adherent to the sternomastoid muscle was a 9-cm. segment of the internal jugular vein. Attached to the lower end of the vein was a well-circumscribed tumour measuring 2.5 x 2 x 3 cm. and, on cross-section, it extended into the vein for a distance of 3 cm. At this point the jugular vein was completely destroyed and replaced by tumour (Fig. 3). The tumour,

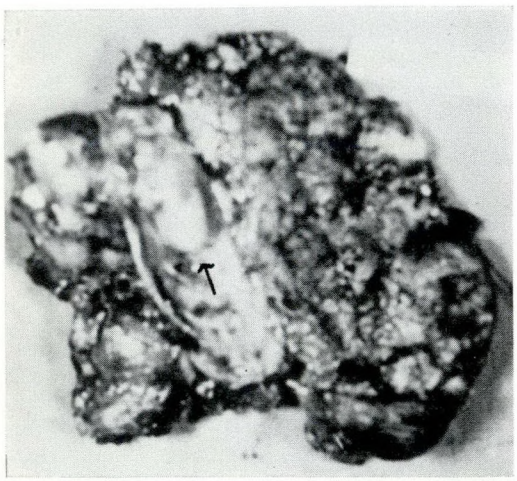

Fig. 3.—Case 2. The specimen in cross-section showing the tumour nodule (arrow) inside the lumen of the vein.

which was greyish-white and fleshy, contained no hemorrhage or necrosis. On microscopy the lesion was composed of interlacing bundles of smooth muscle fibres with areas of nuclear pleomorphism. There were two or three mitotic figures per high power field (Fig. 4). The

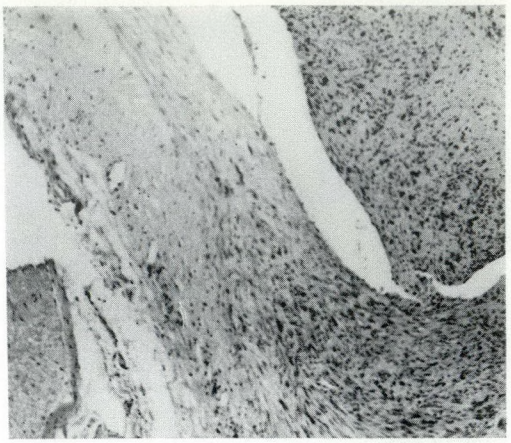

Fig. 4.—Case 2. The wall of the internal jugular vein: the normal wall at the top left merges into the tumour below and at the right (original magnification x 200).

lesion was not encapsulated but was well circumscribed, and numerous finger-like projections extended into the surrounding subcutaneous tissues. The lymph nodes submitted with the specimen were free of tumour. This was a leiomyosarcoma arising from the internal jugular vein.

After an uneventful postoperative course, the patient was well for one year. Then a small lump appeared on the left side of his neck which, on excision biopsy, was a metastatic leiomyosarcoma. Two months later he developed more lumps, one on his back and one on the right side of his neck. At this time his liver function was abnormal and he had hepatomegaly. Radioactive liver scan suggested metastases and a radiograph of the chest showed right costophrenic blunting. He was treated with phenylalanine mustard (melphalan) and discharged. He was readmitted six weeks later with bowel obstruction and liver failure. On June 12, 1968, 16 months after his radical neck dissection, he died in hepatic failure.

Review of the Literature

Primary venous tumours, other than hemangiomas and hemangiosarcomas of the skin and subcutaneous tissues, are most uncommon. In our review of the literature we could find only 49 such tumours. In 1868 Aufrecht described a myoma in the saphenous vein—the first report of a primary venous tumour. Including our two cases, 51 such tumours had been reported up to July 1968. The 49 tumours previously reported are shown in Table I.

TABLE I.—Previously Reported Primary Venous Tumours in Chronological Sequence. Where Known, the Subsequent Course of the Patient is Indicated

Year	*Author*	*Age*	*Sex*	*Tumour*	*Site*	*Comment*
1868	Aufrecht, E.	23	M	Myoma	Saphenous	Excised
1869	Boettcher, A.	30	F	Myoma	Ulnar	Excised
1871	Perl, L.	34	F	Leiomyosarcoma	I.V.C.	At autopsy. No metastases
1896	Cornil, A.	—	—	Myoma	Brachial	Excised
1896	Unruh, F.	1	—	Endothelioma	I.V.C.	At autopsy. No metastases
1897	Brohl, H.	56	F	Round cell sarcoma	Femoral	Excised
1903	Cernezzi, A.	—	M	Fibroleiomyoma	Spermatic plexus	Excised
1903	Oberndorfer, S.	24	F	Endothelial sarcoma	Umbilical	Excised. Died
1904	Picchi, L.	70	M	Enchondroma	Brachial	At autopsy. No metastases
1906	Borchard, P.	44	M	Sarcoma	Saphenous	Excised
1911	Ehrenberg, L.	49	M	Giant cell sarcoma	S.V.C.	At autopsy. Metastases of pleura, heart and retroperitoneum
1913	Niederle, B.	—	—	Leiomyoma	Basilic	Excised
1914	Schnyder, K.	27	F	Leiomyoma	Dorsal metatarsal	Excised
1917	Eccofey, M.	40	M	Fibroleiomyoma	Saphenous branch	Excised
1919	van Ree, A.	42	F	Leiomyosarcoma	Saphenous	Excised. No metastases 15 months later
1920	Razzaboni, G.	64	M	Sarcoma	Saphenous	Excised
1923	Natali, C.	68	M	Fibroleiomyoma	Femoral	Excised
1927	Marri, P.	45	M	Fibroleiomyoma	Axillary	Excised
1928	Melchior, E.	24	F	Fibrosarcoma	I.V.C.	Excised. Died 2 weeks later
1932	Kaplan, S.	3½	—	Leiomyoma	Pulmonary	At autopsy. No metastases
1939	Ausbuttel, F.	51	F	Sarcoma	Pulmonary	At autopsy. Metastases of heart
1940	Hallock, P.	34	F	Leiomyosarcoma	I.V.C.	At autopsy. No metastases
1947	Puig-Sureda, J.	61	F	Leiomyosarcoma	Inferior colic	Excised
1951	Abdullaeva, D. A.	31	F	Leiomyoma	I.V.C.	At autopsy. No metastases
1954	Haug, W. A.	51	M	Leiomyosarcoma	Femoral	Excised. Lung metastases 3 years later
1954	Cope, J. S.[1]	33	F	Leiomyosarcoma	I.V.C.	Excised. Recurred locally
1955	Font, A. J.[2]	50	M	Leiomyosarcoma	Antecubital	Excised
1955	Roussak, N. J.	60	M	Leiomyosarcoma	I.V.C.	At autopsy. No metastases
1955	Johnston, J. H.	67	F	Leiomyosarcoma	Femoral	Excised. Alive 9 months later
1957	Abell, M. R.[3]	45	F	Leiomyosarcoma	I.V.C.	At autopsy. Hepatic metastases
1957	Abell, M. R.[3]	64	F	Leiomyosarcoma	I.V.C.	At autopsy. No metastases
1957	Cumming, A. R.	47	M	Osteogenic sarcoma	Pulmonary	At autopsy. No metastases
1958	DeWeese, J. A.	54	M	Leiomyosarcoma	Saphenous	Excised
1960	Harland, W. A.[4]	64	F	Leiomyosarcoma	I.V.C.	At autopsy
1960	Light, H. G.[5]	42	M	Leiomyosarcoma	Femoral	Excised. No metastases 16 months later
1960	Smout, M. S.[6]	76	F	Leiomyosarcoma	Saphenous	Excised
1960	Thomas, M. A.[7]	64	F	Leiomyosarcoma	I.V.C.	At autopsy
1960	Thomas, M. A.[7]	27	M	Leiomyosarcoma	Internal jugular	Excised. Died from metastases 6 months later
1961	Stout, A. P.[8]	—	—	Sarcoma	Azygos	—
1961	Onerheim, W. O.[9]	83	F	Leiomyosarcoma	I.V.C.	Died 2 weeks after exploration
1961	Kaliteevsky, P. F.	—	—	Leiomyosarcoma	I.V.C.	—
1961	Laufer, A.[10]	57	F	Leiomyosarcoma	I.V.C.	Biopsied. Died
1962	Acherman, L.[11]	61	F	Leiomyosarcoma	I.V.C.	At autopsy. Metastases present
1962	Beaird, J. B.[12]	46	F	Leiomyosarcoma	I.V.C.	At autopsy. Metastases present
1963	Dorfman, H. D.[13]	56	M	Leiomyosarcoma	Saphenous	Excised. Alive 1 year later
1965	Cheek, J. H.[14]	62	F	Leiomyosarcoma	Left jugular	Excised. Two more procedures for recurrences. Alive 5 years later
1966	Lawrence, M. S.[15]	59	F	Leiomyosarcoma	Right iliac	Excised. No metastases 19 months later
1966	Sakurai, O.[16]	54	M	Leiomyosarcoma	Femoral	Excised. No metastases 6 months later
1967	Staley, C. J.[17]	65	F	Leiomyosarcoma	I.V.C.	Excised. No metastases 1 year later

We have reviewed 2800 autopsy reports at the Ottawa Civic Hospital and found no cases of primary venous tumour. Some workers have suggested that peripheral tumours may not be detected at autopsy unless they attained large size before the patient's death.

Discussion

In the present review we included our two cases. Of these 51 cases, the sex of the patient was recorded in 45. There were 20 males and 25 females; the preponderance of women is statistically insignificant. Of the 51 tumours, 38 were malignant and 13 benign. In the malignant group the ratio of women to men was 1.57:1; this was reversed in the benign group —a point we thought significant (Table II).

TABLE II.—Distribution of Benign and Malignant Tumours Between the Sexes

Type of tumour	*Number*	
Benign:	9	
Male	6	
Female	3	Ratio 2:1
Malignant:	36	
Male	14	
Female	22	Ratio 1:1.57

The youngest patient was 12 months old, the oldest 83 years. The incidence of tumours increased with age but most tumours occurred between the ages of 40 and 70. Benign tumours were distributed equally among all ages, but malignant tumours became more frequent with advancing age. For all tumours the mean age of the patients was 48.1: for those with benign tumours alone it was 35.6 and for malignant tumours 52 years.

Seventeen tumours involved the inferior vena cava, most of these were malignant and were discovered at autopsy. Only three of these tumours were resected, one patient being alive one year and one two years after operation. All tumours in the thorax were found at autopsy. All three tumours arising from the jugular veins were malignant and were resected. The longest survival was four years. The peripheral tumours apparently responded better to operation but the results cannot be evaluated because the follow-up is inadequate.

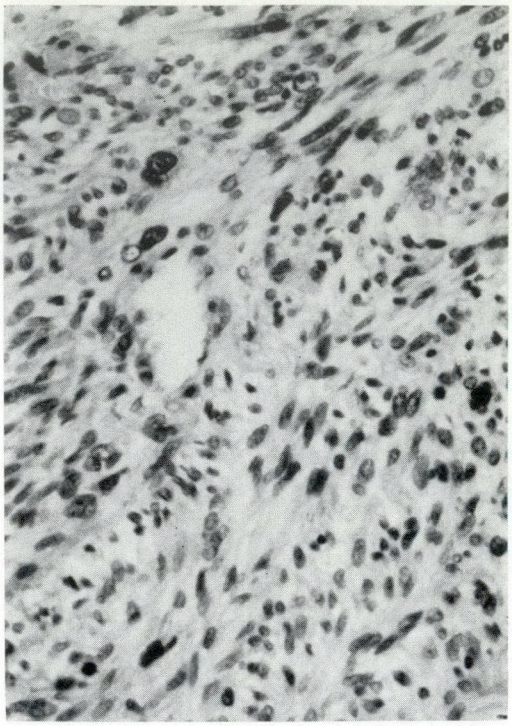

Fig. 5.—Case 1. High power view of the tumour illustrates the wide variation in size and shape of the cells, with some bizarre cell forms arranged in whorls. There are a number of mitotic figures (original magnification x 450).

Microscopically, these tumours range from the benign leiomyomas with regular, elongated cells and no mitoses to aggressive, malignant leiomyosarcomas, composed of large, rather bizarre cells with many abnormal mitotic figures. Between these two extremes, there is a wide range of histological patterns. In general the clinical course correlates well with the presence of bizarre cells and the mitotic activity. Histologically, in both our patients the tumours were malignant. Their clinical courses reflected this—both patients died of their disease.

A typical microscopic field from the first tumour (Case 1) shows variation in cell size, bizarre large cells and numerous mitoses (Fig. 5).

We believe that our two cases represent true primary venous tumours, because in neither case could we find clinical evidence of another primary tumour. Both these tumours seem to have arisen from the vein walls. On microscopy we could demon-

strate transition from the normal wall of the vein to tumour.

Summary

Two patients had leiomyosarcoma, one arising from the long saphenous vein and one from the internal jugular vein. Both were treated surgically and both died of widespread metastases, the first 47 months and the second 18 months after diagnosis. Because primary venous neoplasms other than hemangiomas are rare, we reviewed the literature and found 49 such cases. Our findings during this review are discussed briefly.

We wish to thank Dr. G. W. Dunning for allowing us to present Case 1, and Dr. L. Doubek who referred Case 2 to the Vascular Surgery Service. We are also indebted to the Ottawa Civic Hospital Division of the Ontario Cancer Foundation for their invaluable assistance in preparing this paper.

References

1. Cope, J. S. and Hunt, C. J.: Leiomyosarcoma of the inferior vena cava, *A.M.A. Arch. Surg.*, **68:** 752, 1954.
2. Font, A. J. and Noer, H. R.: Primary leiomyosarcoma of antecubital vein; report of case with review of literature, *Grace Hosp. Bull. (Detroit)*, **33:** 35, 1955.
3. Abell, M. R.: Leiomyosarcoma of inferior vena cava; review of literature and report of two cases, *Amer. J. Clin. Path.*, **28:** 272, 1957.
4. Harland, W. A., Clamen, M. and Rodriguez, V. M.: Leiomyosarcoma of inferior vena cava with clinical features of Chiari's syndrome, *Canad. Med. Ass. J.*, **83:** 1064, 1960.
5. Light, H. G., Peskin, G. W. and Ravdin, I. S.: Primary tumors of venous system, *Cancer*, **13:** 818, 1960.
6. Smout, M. S. and Fisher, J. H.: Leiomyosarcoma of saphenous vein, *Canad. Med. Ass. J.*, **83:** 1066, 1960.
7. Thomas, M. A. and Fine, G.: Leiomyosarcoma of veins; report of two cases and review of the literature, *Cancer*, **13:** 96, 1960.
8. Stout, A. P. and Hill, W. T.: Sarcomas of the soft tissues, *CA*, **11:** 210, 1961.
9. Onerheim, W. O. and Tesluk, H.: Leiomyosarcoma of inferior vena cava, *Arch. Surg. (Chicago)*, **82:** 395, 1961.
10. Laufer, A. and Plaschkes, J.: Primary leiomyosarcoma of inferior vena cava, *Path. Microbiol. (Basel)*, **24:** 72, 1961.
11. Clinico-pathologic Conference: Unusual cause of rapidly progressive hepatic failure, *Amer. J. Med.*, **32:** 599, 1962.
12. Beaird, J. B. and Scofield, G. F.: Budd-Chiari syndrome. Hepatic vein occlusion due to leiomyosarcoma primary in the inferior vena cava, *Arch. Intern. Med. (Chicago)*, **110:** 435, 1962.
13. Dorfman, H. D. and Fishel, E. R.: Leiomyosarcoma of greater saphenous vein, *Amer. J. Clin. Path.*, **39:** 73, 1963.
14. Cheek, J. H. and Nickey, W. M.: Leiomyosarcoma of venous origin, *Arch. Surg. (Chicago)*, **90:** 396, 1965.
15. Lawrence, M. S., Crosby, V. G. and Ehrenhaft, J. L.: Leiomyosarcoma of the right iliac vein; case report, *Ann. Surg.*, **164:** 924, 1966.
16. Sakurai, O., Toda, A. and Morimoto, K.: Primary leiomyosarcoma within the femoral vein, *Clin. Orthop.*, **44:** 197, 1966.
17. Staley, C. J. *et al.*: Leiomyosarcoma of the inferior vena cava, *Amer. J. Surg.*, **113:** 211, 1967.

Résumé

A l'exception des hémangiomes et des hémangiosarcomes, les néoplasmes veineux primaires sont rares. Jusqu'à 1967, on n'en avait signalé que 49 cas. Le siège le plus courant de ces tumeurs était la veine cave inférieure et la majorité des tumeurs étaient de nature maligne. Ces tumeurs malignes étant traitées, le pronostic était sombre. Les auteurs ont ajouté à cette liste deux cas de leur pratique personnelle. Le premier, homme de 68 ans, présentait sur la cuisse une "bosse" qui était fixée aux tissus profonds. On excisa la tumeur et on découvrit qu'ils s'agissait d'un léiomyosarcome ayant prise naissance sur la veine saphène interne. Opéré, il se sentit bien pendant deux ans, puis présenta une tumeur semblable sur la face. Il décéda, quatre ans après le diagnostic originel, d'insuffisance hépatique causée par des métastases sévères du foie. Le second malade, homme de 37 ans, avait une "bosse" asymptomatique sur le côté droit du cou, qui était apparue neuf mois plus tôt et qui augmentait de volume. Il s'agissait également d'un léiomyosarcome ayant son point de départ sur la veine jugulaire interne. On pratiqua une résection radicale du côté droit du cou. Bien portant pendant un an, il présenta ensuite de multiples métastases et mourut, 16 mois après l'opération, d'insuffisance hépatique causée par une atteinte métastatique du foie.

LIPOGRANULOMA OF BONE: REPORT OF THREE CASES*

S. J. TREDWELL, M.D., K. S. MORTON, B.A., M.Sc., M.D., C.M., F.R.C.S.[C], F.A.C.S. and P. S. VASSAR, M.B., B.S., M.R.C.S.[Eng.], F.C.A.P., M.C.Path.[Eng.],
Vancouver, B.C.

Among the less common circumscribed radiolucencies of bone is the histiocytosis-X group of lesions described by Lichtenstein[1] in 1953. He proposed that the hitherto separately described Letterer-Siwe disease, Hand-Schüller-Christian disease and eosinophilic granuloma be included as differing aspects of histiocytic involvement which he designated histiocytosis-X. In 1966 Gresham, Melcher and Whitelaw[2] described five cases of a lesion they named lipogranuloma of bone and recognized the similarity of this condition to the histiocytosis-X group.

Lipogranuloma occurs in the marrow cavity. Grossly, it is a cyst filled with brownish-yellow, semisolid material. Histologically, the lesion is composed of lipid-engorged histiocytes. Hemosiderin deposits are usually present and the outer fibrous capsule contains cholesterol clefts and foreign-body giant cells.

In the 15 years 1951 to 1965, three patients with lipogranuloma of bone have been seen at the Vancouver General Hospital.

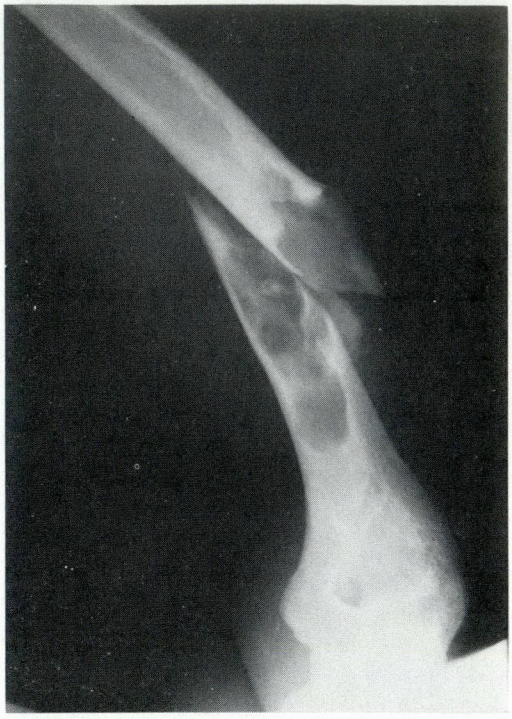

Fig. 1.—Case 1. Multiloculated, radiolucent lesion of the humerus with a pathologic fracture.

Case Reports

Case 1.—A.M., a 55-year-old labourer, was admitted to the Orthopedic Service on March 27, 1951 because he had fractured his left humerus while pushing a wheelbarrow. His hemoglobin was 16.6 g./100 ml., leukocyte count was 7400/c.mm., alkaline phosphatase 4 King-Armstrong (KA) units, serum calcium 9.8 mg./100 ml., serum phosphate 5.6 mg./100 ml., acid phosphatase 3.3 KA units and Bence Jones proteins were not present.

Radiographs (Fig. 1) revealed a multiloculated, radiolucent lesion involving the lower third of the shaft of the humerus through which a fracture had occurred. It had not expanded the cortex. On a radiographic survey of the chest, skull and pelvis, we found no additional lesions.

On April 5 the lesion was curetted, packed with autogenous iliac bone chips and the fracture was fixed with screws. The patient's postoperative course was uneventful. The gross specimen consisted of a friable, reddish-brown to dirty-yellow material. Microscopically, there were numerous cholesterol clefts and foreign-body giant cells containing cholesterol (Fig. 2). There was much fibroblastic proliferation and many histiocytes were filled with hemosiderin.

His cast was removed on August 6 and by March 19, 1952, one year after initial treatment, he was advised to return to work. Four years later his only complaint was referable to the left wrist. Radiographs of the original lesion (Fig. 3) showed some residual radiolucency. Seven years after diagnosis he remained well and no further treatment was advised.

Case 2.—D.D., a 54-year-old fisherman, was admitted to the Orthopedic Service on November 1, 1965 following an acute flexion-extension injury to his neck. He complained of diffuse pain about the right shoulder. A history of recurrent, right renal calculi was obtained.

*From the Departments of Pathology and Surgery (Orthopedics), University of British Columbia, Vancouver, B.C.

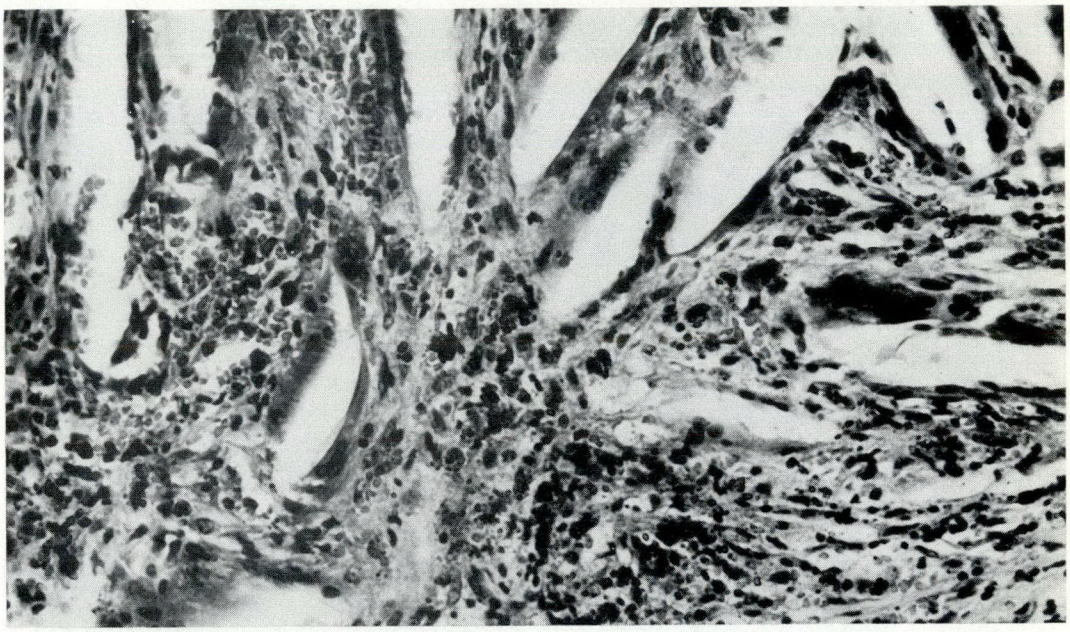

Fig. 2.—Case 1. Cholesterol clefts and foreign-body giant cells in fibroblastic stroma containing histiocytes and hemosiderin (x 250).

Fig. 3.—Case 1. Radiographic appearance four years after operation.

On radiographic examination, he had minimal degenerative changes of the cervical spine and an incidental, 1.5-cm., radiolucent lesion related to the spine of the scapula near the acromion process (Fig. 4). Skeletal survey did

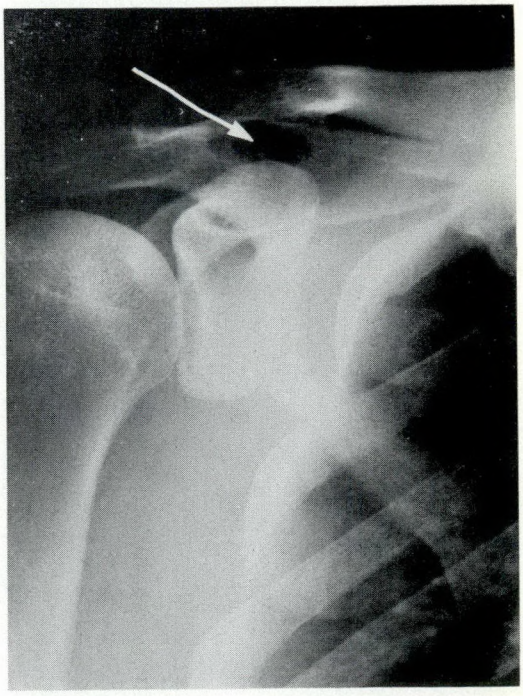

Fig. 4.—Case 2. Radiolucent lesion in the spine of the scapula (arrow).

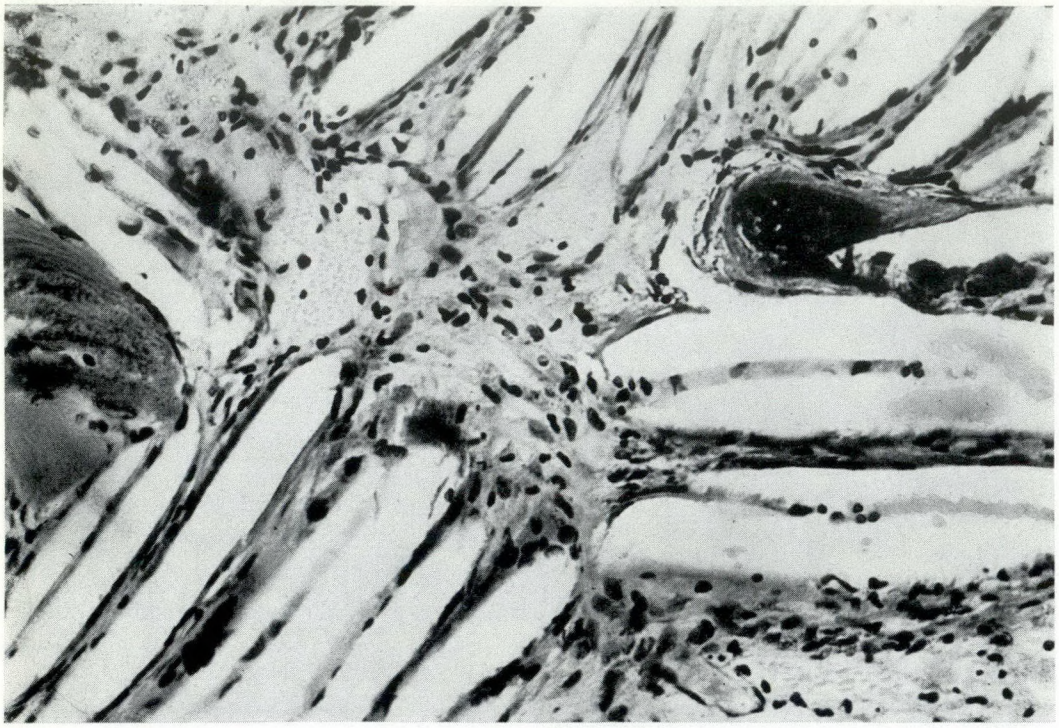

Fig. 5a

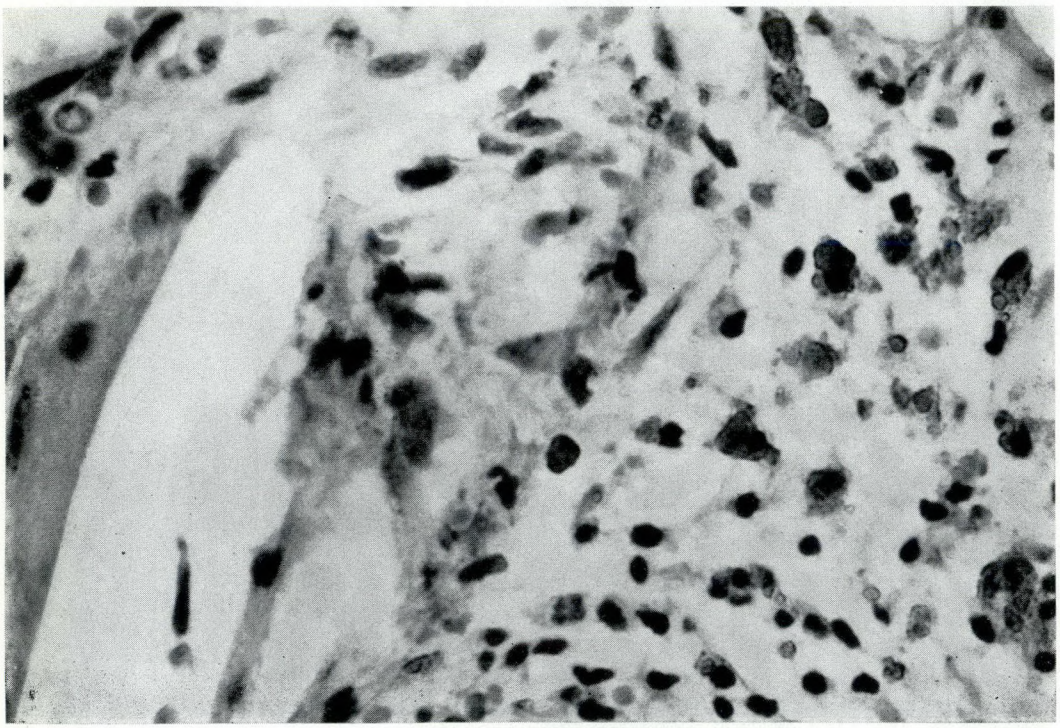

Fig. 5b

Fig. 5.—Case 2. (a) Numerous cholesterol clefts and histiocytes with an occasional giant cell (x 250). (b) High power magnification to show hemosiderin granules in macrophages and histiocytes (x 890).

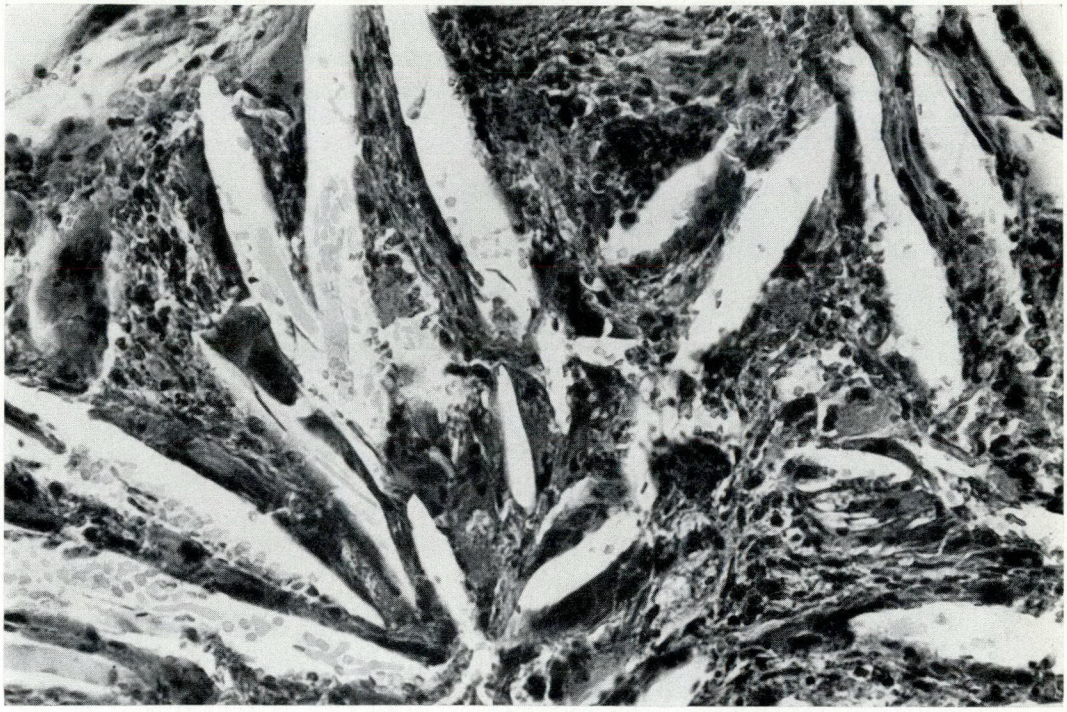

Fig. 6a

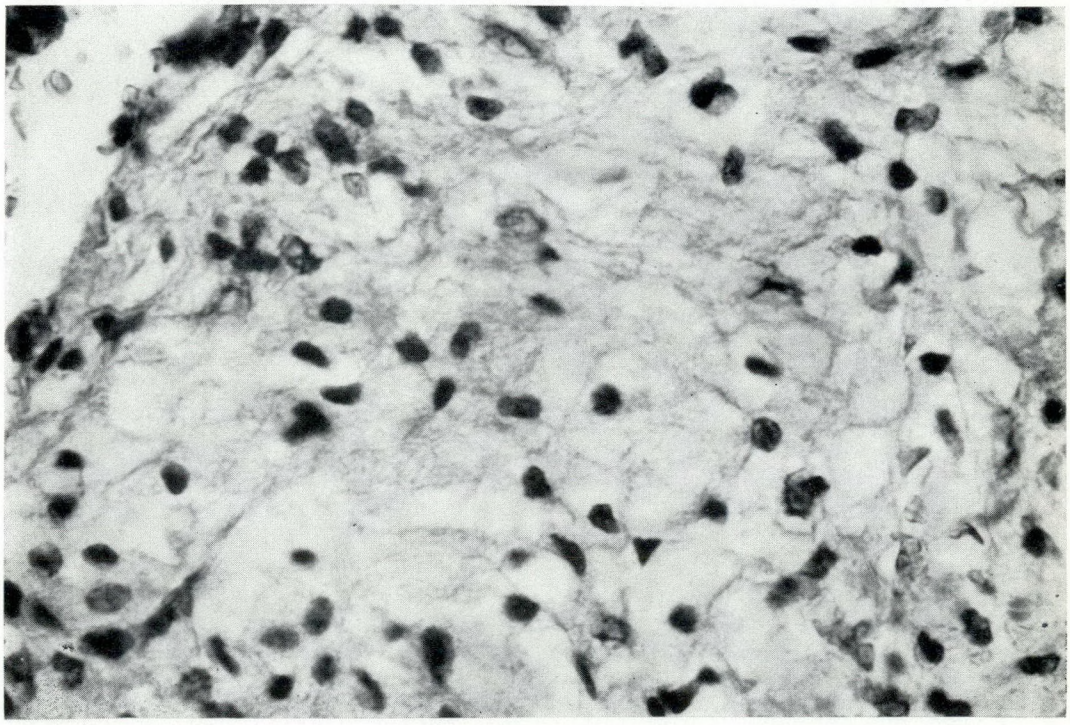

Fig. 6b

Fig. 6.—Case 3. (a) Fibrous connective tissue surrounds typical cholesterol clefts and giant cell reaction. (b) High power magnification illustrating foamy histiocytes (x 890).

not reveal any additional lesions. In the opinion of the radiologist, this lesion was either a secondary carcinoma, multiple myeloma or eosinophilic granuloma.

His hemoglobin was 14.5 g./100 ml., leukocyte count was 7800/c.mm., alkaline phosphatase 12 KA units, acid phosphatase 1.9 KA units, serum phosphate 1.4 mg./100 ml. and serum cholesterol 370 mg./100 ml. The urine contained calcium oxalate crystals but no Bence Jones protein.

The lesion was curetted. The gross specimen was soft and yellow-brown. On microscopic examination (Fig. 5) we saw the characteristic cholesterol clefts surrounded by foreign-body giant cells and histiocytes containing hemosiderin.

His subsequent course was uneventful except for recurring symptoms related to his renal calculi.

Case 3.—J.L., a 37-year-old man, presented with a history of progressive drooping of the right eyelid and limitation of upward gaze for six months. He was admitted to the Neurosurgical Service in November 1953. The right eye was depressed and he had a right ptosis. The right pupil was 3 to 4 mm. lower than the left. Extraocular movements were intact and he had no proptosis, no chemosis and no corneal ulceration. Fundi and optic discs were normal. Radiographs revealed a destructive lesion of the right bony orbit.

At operation a right frontal bone flap was turned and an extraocular mass was excised. Adjacent bone was curetted. The gross specimen was yellow-orange and friable. On microscopic examination (Fig. 6) the tissue was composed of fibrous connective tissue with cholesterol clefts and foreign-body giant cells. There were some hemosiderin deposits and areas with foamy histiocytes.

His postoperative course was uneventful; he was last seen when he was discharged from hospital two weeks after operation.

Discussion

The five cases of lipogranuloma of bone reported by Gresham, Melcher and Whitelaw[2] in January 1966 occurred in the long bones of adults. They were described as inflammatory reactions to necrotic fat, well demarcated in cancellous bone with occasional surrounding sclerosis. These authors related the lesion to histiocytosis-X but did not explain their choice of the description *lipogranuloma*, although, undoubtedly, they recognized the characteristic histopathology of lipogranulomatosis.[3]

References to lesions of this type are difficult to trace in the literature because of varying terminology and the inclusion of lipogranuloma with the histiocytoses, unicameral bone cysts and lipid storage disease. Ayres and Cameron[4] described four cysts of the os calcis that had a microscopic appearance strikingly similar to lipogranuloma of bone. All were in young adults. In reviewing a further 22 cases from the literature, they recognized cholesterol crystals and giant cell reaction in at least five.

Golden and Richards[5] described two cases with some similarity to lipogranuloma of bone. These were multiple lesions in long bones adjacent to joints and were associated with rheumatoid arthritis. They referred to the condition as "xanthogranulomatous disease of bone".

Our three patients were men, aged 55, 54 and 37 years; the lesions involved the humerus, scapula and frontal bone. The histological appearance—cholesterol clefts surrounded by foreign-body giant cells with hemosiderin-filled histiocytes—is that described by Gresham, Melcher and Whitelaw.[2] Our patients and theirs were treated by curettage with or without bone grafting and, on short follow-up, this treatment appeared to be effective.

The observations of Gresham, Melcher and Whitelaw,[2] which related lipogranuloma of bone to histiocytosis-X, prompted us to review our cases in this group. During the 15-year period 1951 to 1965, 76 cases of the histiocytosis-X group, lipogranuloma and lipid-storage disease have been recorded in our centre (Table I).

Lichtenstein[6] suggests that histiocytosis-X may be a response to a peculiar type of

TABLE I.—Seventy-Six Cases of Histiocytosis-X, 1951 to 1965

Diagnosis	*Number of cases*	*Number with bone involvement*
Histiocytosis-X (undesignated)	7	0
Letterer-Siwe disease	8	3
Hand-Schüller-Christian disease	5	4
Eosinophilic granuloma	40	36
Lipogranuloma of bone	3	3
Lipid-storage disease (Gaucher's, Niemann-Pick)	13	3

infection in which eosinophilic granuloma represents an early localized reaction, while Letterer-Siwe and Hand-Schüller-Christian diseases represent the acute and chronic systemic forms. This view is somewhat similar to that of of Gresham, Melcher and Whitelaw.[2]

Lipogranuloma may or may not belong to the histiocytosis-X group. Common to these lesions is an inflammatory proliferative reaction. Though lipogranuloma does not present the progressive picture seen in some of the histiocytosis-X group, neither does eosinophilic granuloma. The presence of hemosiderin in lipogranuloma, found in all three of our cases and all five of those reported by Gresham,[2] is not consistent with histiocytosis-X. Lipogranuloma might represent conversion of eosinophilic granuloma by secondary lipidization, that is, conversion of the histiocytes to lipophages. Jaffe[7] believes that eosinophilic granuloma heals by resolution and not by lipidization. Lichtenstein[6] reports that, in some cases of Letterer-Siwe disease, the rapidly forming histiocytes in the new skeletal lesions may become foamy almost as quickly as they are formed. This observation indicates that lipidization does not represent a secondary change.

Lipogranuloma must be differentiated from the lipid-storage diseases, Gaucher's and Niemann-Pick—conditions that have a distinct histological appearance as does their cholesterol analogue, xanthoma tuberosum. Non-osteogenic fibroma (metaphyseal fibrous defect), a more common lesion with radiological and pathological similarities, may show lipid-filled macrophages and hemosiderin, but its giant cells are osteoclasts and it has no cholesterol.

Summary

Three cases of lipogranuloma of bone are described distinguishing this lesion from but relating it to the histiocytosis-X group of lesions referred to by Lichtenstein.

Lipogranuloma, so named by Gresham, Melcher and Whitelaw in 1966, is a circumscribed radiolucency in the marrow cavity appearing grossly as a cyst filled with brownish-yellow, semisolid material. Histologically, it is composed of lipid-engorged histiocytes with hemosiderin deposits. Striking are the cholesterol crystal clefts with surrounding foreign-body giant cells.

Its similarities to lipid-storage diseases and also the much more common non-osteogenic fibroma are also discussed.

References

1. Lichtenstein, L.: Histiocytosis X. Integration of eosinophilic granuloma of bone, "Letterer-Siwe disease" and "Schüller-Christian disease" as related manifestations of a single nosologic entity, *A.M.A. Arch. Path.*, **56:** 84, 1953.
2. Gresham, G. A., Melcher, D. H. and Whitelaw, R. A.: Lipogranuloma of bone, *J. Clin. Path.*, **19:** 65, 1966.
3. Anderson, W. A. D.: Pathology, 4th ed., The C. V. Mosby Company, St. Louis, 1961.
4. Ayres, W. W. and Cameron, B. M.: Cysts of the os calcis, *U.S. Armed Forces Med. J.*, **8:** 1102, 1957.
5. Golden, G. N. and Richards, H. G.: Xanthogranulomatous disease of bone with polyarthritis; report of two cases, *J. Bone Joint Surg.* [*Brit.*], **35B:** 275, 1953.
6. Lichtenstein, L.: Bone tumors, 3rd ed., The C. V. Mosby Company, St. Louis, 1965.
7. Jaffe, H. L.: Tumors and tumorous conditions of the bones and joints, Lea & Febiger, Philadelphia, 1958.

Résumé

Les auteurs présentent ici trois cas de granulome lipidique, faisant une distinction entre cette pathologie et la réticulose X de Lichtenstein, tout en l'y reliant cependant.

Le granulome lipidique ou lipogranulome comme l'ont nommé Gresham, Melcher et Whitelaw en 1966, se présente à la radiographie sous forme d'une région translucide circonscrite dans la cavité médullaire, ayant l'apparence approximative d'un kyste rempli d'une substance semi-solide, jaune-brunâtre. Au point de vue histologique, cette masse est composée d'hystiocytes farçis de lipides avec dépôts d'hémosidérine. Les particularités les plus frappantes sont les fentes résiduelles aux cristaux de cholestérol ainsi que les cellules géantes agissant comme corps étranger qui les entourent.

On attire l'attention du lecteur sur ses similitudes avec les maladies par dépôt lipidique et avec le fibrome non ostéogénique, beaucoup plus courant.

DIAPHRAGMATIC DISRUPTION IN MAJOR THORACIC TRAUMA: A REVIEW OF 16 CASES*

L. P. STERNS, M.D., M.Sc., F.R.C.S.[C], F.A.C.S., N. K. JENSEN, M.D., F.A.C.S., W. R. SCHMIDT, M.D., F.A.C.S., J. J. GARAMELLA, M.D., Ph.D., F.A.C.S. and M. F. LYNCH, M.D., F.A.C.S., *Minneapolis, Minn., U.S.A. and Edmonton, Alta.*

If patients who have sustained major trauma to the thorax or upper abdomen show signs and symptoms of serious organ involvement that cannot be attributed to the obvious injury, disruption of the diaphragm should be suspected. This report describes 16 such patients seen over the past 15 years and emphasizes that this potentially correctible lesion must be kept in mind.

Selection of Cases

All 16 patients were treated either at Northwestern Hospital, Minneapolis or the University of Alberta Hospital, Edmonton; 13 were male and three were female. They ranged in age from 12 to 64 years (Table I). In 12, the injuries resulted from auto-

TABLE I.—Traumatic Rupture of the Diaphragm (16 Patients)

Case number		*Patient*	*Sex*	*Age*	*Side of rupture*	*Cause*
Minneapolis:	1	G.E.	F	38	Left	Auto
	2	L.A.	F	35	Left	Auto
	3	C.J.	M	60	Left	Fall
	4	A.W.	M	30	Left	Crushed by horse
	5	A.S.	M	25	Left	Auto
	6	V.E.	M	12	Left	Auto
	7	B.K.	M	15	Left	Auto
	8	J.G.	M	33	Right	Fall
	9	S.B.	M	42	Right	Auto
	10	K.A.	M	50	Left	Auto
Alberta:	1	E.K.	M	23	Left	Auto
	2	N.D.	M	64	Left	Tractor
	3	M.D.	F	13	Left	Auto
	4	W.D.	M	58	Left	Auto
	5	G.N.	M	30	Left	Auto
	6	R.C.	M	27	Right	Auto

mobile collisions, one from a tractor accident and two from falls. The final patient had an accident in which a horse fell across his chest.

At operation the diaphragm was disrupted on the right in three patients and on the left in the remaining 13. In these 13, the abdominal contents herniated into the left pleural space. In five of these the spleen was also ruptured and was removed at operation.

In all three patients in whom the right diaphragm was ruptured, problems due to extensive peripheral detachment of the right leaf of the diaphragm as well as herniation of the right lobe of the liver into the right hemithorax made operative repair necessary. Of the 13 with injury to the left diaphragm, repair in 10 was done through a standard left thoracotomy. Two required a thoracoabdominal incision, and the thirteenth was repaired through an abdominal approach. As noted above, in all 13, the abdominal contents, especially stomach, small bowel, spleen and splenic flexure of the colon, migrated into the left pleural space. All the left diaphragm tears were repaired by direct suture. In four of these patients who had more extensive injuries to the chest, a tracheotomy was done to facilitate respiration during operation and tracheobronchial toilet after operation.

Representative Case Reports

Case Alberta 1.—In an automobile accident a 23-year-old man sustained a steering-wheel

*From the Division of Thoracic Surgery, Northwestern Hospital, Minneapolis, Minn. and the Division of Thoracic and Cardiovascular Surgery, University Hospital, Edmonton, Alta.

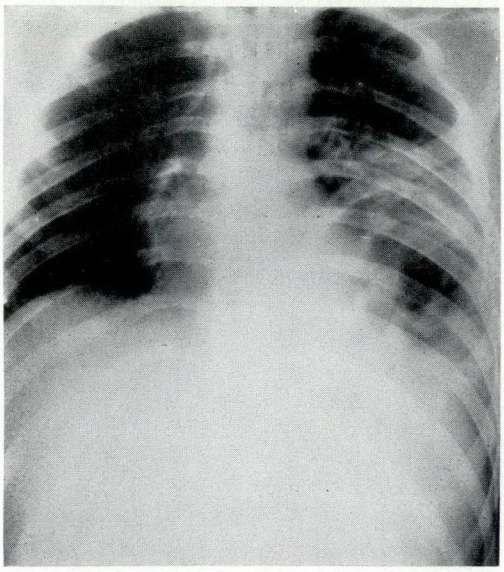

Fig. 1.—Case Alberta 1. Chest film of a 23-year-old man after an automobile accident. He had a radial tear in the left leaf of the diaphragm, and the spleen and omentum had herniated into the left hemithorax.

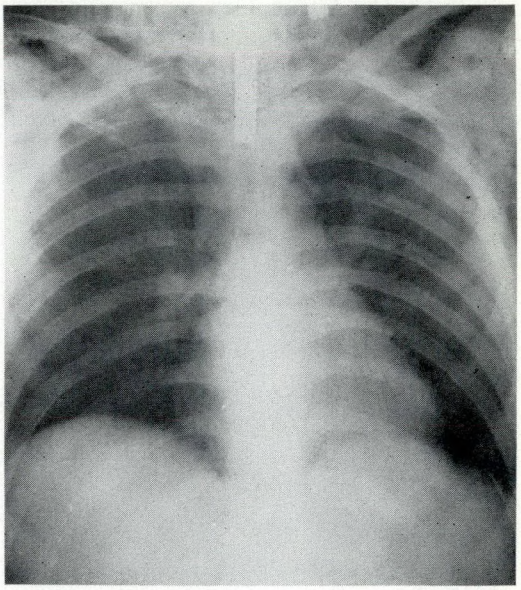

Fig. 2.—Case Alberta 1. Appearance of the chest after the rent in the left leaf of the diaphragm had been repaired. He did not require splenectomy and the defect was repaired by primary suture.

injury to the left chest. On admission chest films (Fig. 1) he had abdominal organs in the left pleural space. He was operated upon immediately. When the left thorax was opened through the sixth interspace, we found that the spleen and omentum had herniated through a radial tear in the left diaphragmatic leaf. The spleen was intact, and it and the other viscera were returned to the peritoneal cavity and the defect was sutured. After operation the chest film was normal (Fig. 2). At follow-up, the patient is doing well.

Case Alberta 2.—This 64-year-old farmer, who was severely injured when struck by a

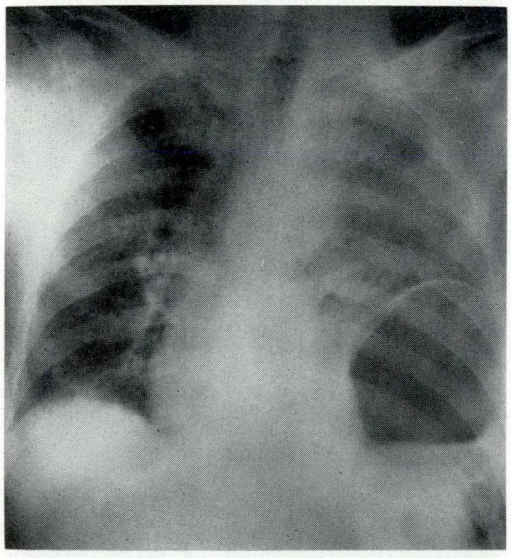

Fig. 3.—Case Alberta 2. Admission chest film. A 64-year-old farmer had been struck by a tractor. The gas-filled abdominal contents fill the left hemithorax.

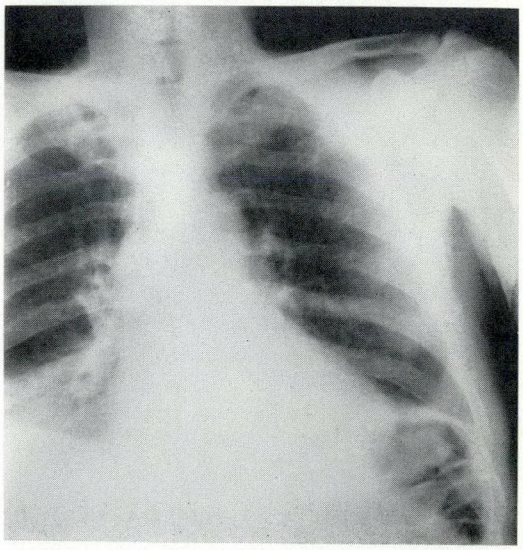

Fig. 4.—Case Alberta 2. Appearance of the chest following successful repair. This man had a complete tear across the dome of the left diaphragm and, at operation, we found the stomach and small bowel in the left pleural space.

tractor, was admitted to hospital complaining of left chest pain and extreme dyspnea. He had abdominal contents in the left pleural space (Fig. 3). On left thoracotomy the dome of the left leaf of the diaphragm was torn completely across. This tear extended anteriorly into the right pleural space. After returning the stomach and small bowel to the peritoneal cavity the tear was repaired.

Chest films after operation (Fig. 4) showed good pulmonary markings in all lung fields. The patient made an uneventful recovery.

Case Alberta 5.—Four days before his admission to the University Hospital in Edmonton, this 30-year-old man had been involved in a serious car accident. Because he had extreme dyspnea, a tracheotomy was performed

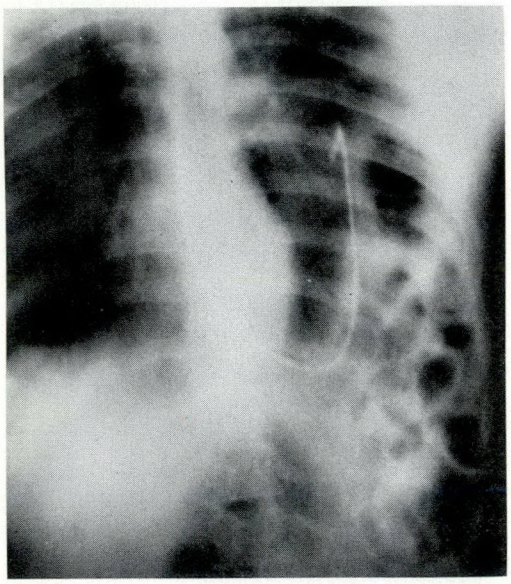

Fig. 5.—Case Alberta 5. This 30-year-old man had been in an automobile accident four days before he was admitted to University Hospital, Edmonton. The nasogastric tube lies in the stomach which is in the left pleural space.

immediately. On admission, the chest film showed that bowel was present in the left pleural cavity. This was confirmed by passing a nasogastric tube (Fig. 5). Six days later he was taken to the operating room where, through an abdominal approach, a radial tear in the left leaf of the diaphragm was repaired, after returning the small bowel and stomach to the abdomen. His subsequent course has been uneventful.

Case Alberta 6.—In 1959 this 27-year-old man sustained injuries to the right side of his chest in an automobile accident. Four years later, in 1963, he sought medical advice because of vague abdominal pains and discomfort in the right upper quadrant that had been present for the previous 18 months. His bowel function was also irregular. Chest films (Fig. 6)

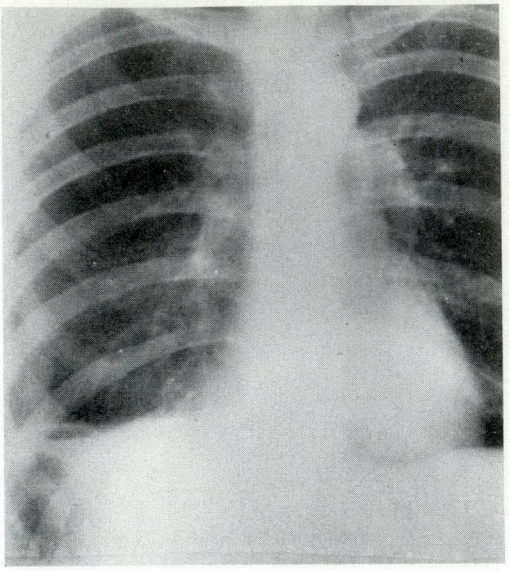

Fig. 6.—Case Alberta 6. A 27-year-old man had been involved in an automobile accident four years before. During examination for vague abdominal pains and irregular bowel function, this chest film was made. It shows a gas-filled shadow in the right base.

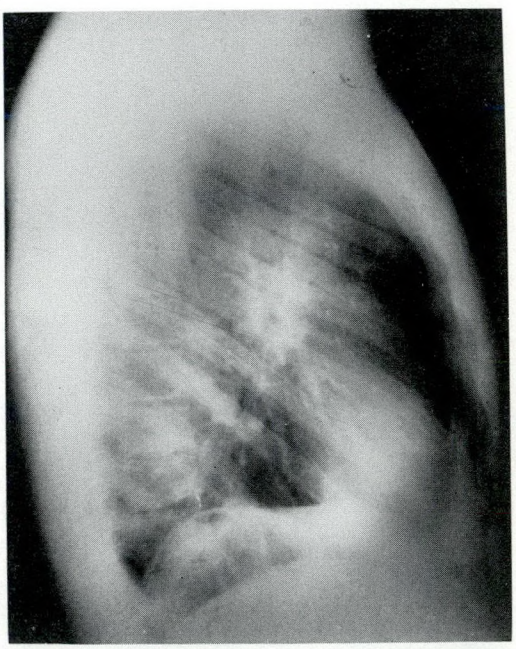

Fig. 7.—Case Alberta 6. Lateral chest film showing the gas-filled viscus in the right lower posterior hemithorax.

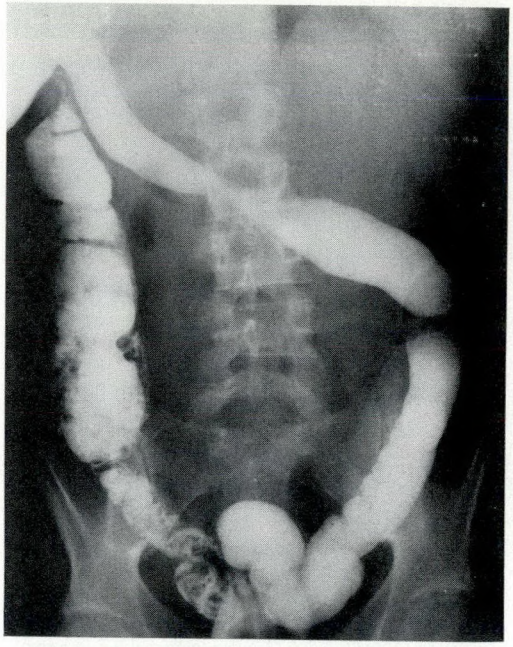

Fig. 8.—Case Alberta 6. Barium enema showing distortion of the colon. The hepatic flexure extends above the level of the diaphragm.

showed a gas-filled shadow at the right base. Lateral roentgenograms (Fig. 7) confirmed this. A barium enema showed that the hepatic flexure of the colon extended above the right leaf of the diaphragm (Fig. 8). Through a right thoracotomy, a localized peripheral tear in the right leaf of the diaphragm was repaired. Fig. 9 shows his postoperative film to be satisfactory, save for some blunting of the right base. He has been asymptomatic since operation.

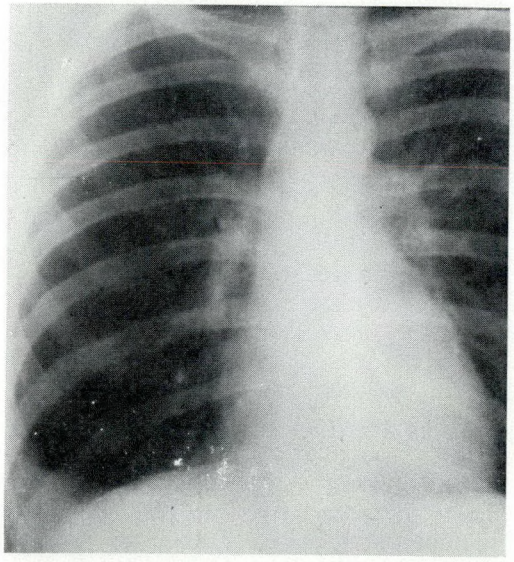

Fig. 9.—Case Alberta 6. Chest film after operation. The viscera have been returned to the abdominal cavity. There is minimal residual blunting at the right base.

**Case* 9.—A 42-year-old man was admitted to Northwestern Hospital, Minneapolis, nine days after he had been in an automobile accident. At the time of injury he had been admitted to a local hospital where roentgenograms showed fractures of the eighth and ninth ribs posteriorly on the right side. We suspected further fractures of the right lower ribs but could not demonstrate them because the lower one-third of the right hemithorax was obscured by subcutaneous emphysema. He had no pneumothorax. Over the next seven days the density on the right side increased and the mediastinal structures shifted to the left. Because he had increasing dyspnea, he was referred to the Northwestern Hospital. On admission he was markedly dyspneic and had shallow respirations 24/min. The right chest was dull to percussion. Below the right nipple bowel sounds could be heard. The chest film (Fig. 10) showed that the normal pulmonary structures were obliterated below the level of the fourth right lateral interspace and, on

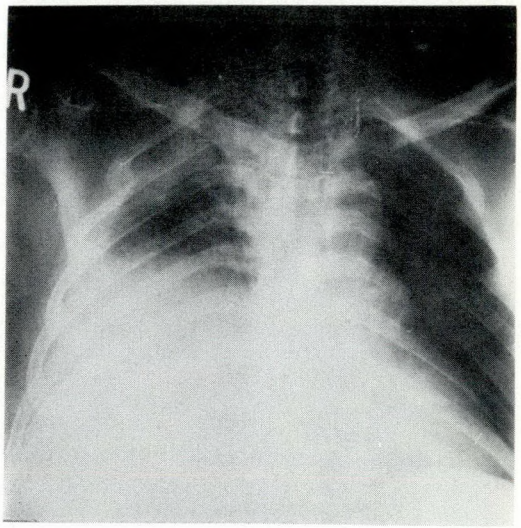

Fig. 10.—Case 9. Admission film of a 42-year-old man nine days after an automobile accident. Normal pulmonary structures have been obliterated below the level of the fourth right lateral interspace.

*Republished by permission from *Dis. Chest,* **51:** 205, 1967.

aspiration, we obtained 50 c.c. of frankly bloody fluid. Over the next few hours, this density increased. On the flat film of the abdomen there was no liver shadow in the right upper quadrant (Fig. 11). We did a right

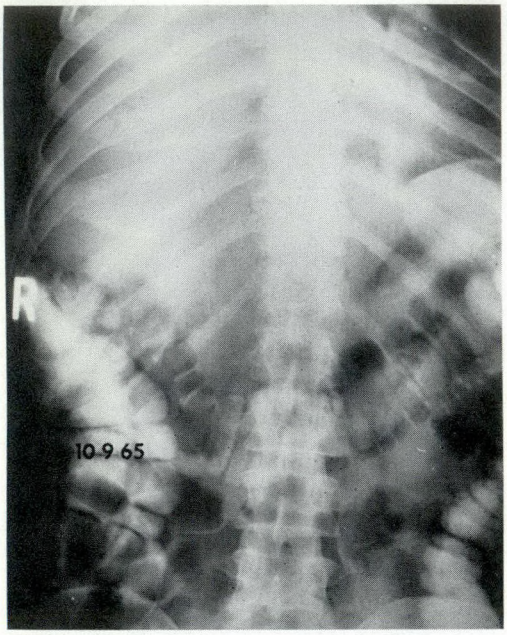

Fig. 11.—Case 9. Abdominal film. There is no hepatic shadow in the right upper quadrant. At operation the right lobe of the liver had herniated into the right pleural space.

thoracotomy excising the eighth rib and, upon opening the pleural space, the right lobe of the liver presented into the wound. The entire right lobe and part of the left lobe of the liver, and several loops of small bowel were all in the right pleural space. The dome of the liver reached the level of the fourth rib anteriorly. The peripheral attachments of the right leaf of the diaphragm had been completely avulsed from the region of the fractured ribs. The tear extended from the foramen of Morgagni anteriorly to the costovertebral junction posteriorly. The retracted right diaphragm was found folded against itself in the medial one-third of the right pleural space. By rotating the anterior edge of the right lobe of the liver forward and medially, we returned the abdominal contents to their proper position. The torn costal edge of the diaphragm was circumferentially attached to the ninth right rib by interrupted mattress sutures of 00 black silk brought through the entire thickness of the chest wall and tied over rubber tubing. Even though the right leaf of the diaphragm was still elevated, his respiratory function improved markedly. Four months later this patient's chest was clear, his vital capacity was 2500 c.c. in one second, total 3000 c.c., and the right leaf of the diaphragm was beginning to move.

Results

Fourteen of the 16 patients in this series recovered from the effects of their accident and subsequent operations and are now well and active. One man (Case 3) withstood his operation but on a recent follow-up we found that he has limited exercise tolerance. His chest films show that he has fair diaphragmatic movement; hence, his easy fatigability may be due to his age (60 years). Another patient (Case Alberta 5) has good respiratory function but, because of a spinal injury at the time of his accident, is paraplegic.

We have followed these patients as long as 14 years after repair. Movement of the involved leaf of the diaphragm, determined by chest fluoroscopy, was "fair" in four and "good" in the remaining 12. None of the 12 with good diaphragmatic excursion have dyspnea, but the four with impaired movement have some shortness of breath with activity.

Discussion

Schwindt and Gale[1] have divided the signs and symptoms of traumatic rupture of the diaphragm into three phases: acute, interval and latent. As in several of our cases, acute rupture is a well-defined entity which presents as a surgical emergency. In all instances of acute rupture the left leaf separates and the intra-abdominal contents are displaced into the pleural space. In many of these patients the spleen is injured and the resulting shock and dyspnea make immediate operation necessary. With early operation these patients usually recover without incident.

Schwindt's second phase, interval rupture of the diaphragm, is well demonstrated by our Case Alberta 6. In this phase, the patient survives the immediate trauma and recovers sufficiently to leave hospital. However, over the subsequent months or years, he continues to have vague symptoms and, after further investi-

gations, the ruptured diaphragm is recognized and repaired. In most of these patients, the vague symptoms point to the gastrointestinal tract[2] and appropriate roentgenologic studies usually lead to the correct diagnosis.

In this series we encountered no latent-phase patients (those presenting with delayed obstruction or strangulation of an incarcerated viscus). However, delayed and catastrophic strangulation can follow either direct or indirect diaphragmatic trauma.[1, 3]

As emphasized in the 16 cases presented here, the attending physician or surgeon should keep diaphragmatic injury in mind constantly when examining patients with thoracic or upper abdominal trauma. Once such rupture has been diagnosed, the patient should be supported with transfusions, a tracheostomy done if he has respiratory distress and he should be prepared for operation at once. As shown here, these traumatic ruptures can be repaired with an acceptable morbidity and good return of function achieved.

Conclusions

In 16 patients with rupture of the diaphragm the rupture was repaired: all survived. In all but one, the torn leaf was approached through a thoracotomy or a thoracoabdominal incision. Fourteen of these patients are well and active. Of the last two, one has limited exercise tolerance and the last is paraplegic.

References

1. Schwindt, W. D. and Gale, J. W.: Late recognition and treatment of traumatic diaphragmatic hernias, *Arch. Surg. (Chicago)*, **94:** 330, 1967.
2. Ebert, P. A., Gaertner, R. A. and Zuidema, G. D.: Traumatic diaphragmatic hernia, *Surg. Gynec. Obstet.*, **125:** 59, 1967.
3. Sullivan, R. E.: Strangulation and obstruction in diaphragmatic hernia due to direct trauma; report of two cases and review of the English literature, *J. Thorac. Cardiovasc. Surg.*, **52:** 725, 1966.

Résumé

Seize malades, dont l'âge variait de 12 à 64 ans, avaient subi un traumatisme thoracique majeur et subséquemment, une rupture du diaphragme. Dans tous ces cas sauf deux, ces blessures résultaient d'accidents d'automobile ou étaient survenues sur la ferme. Les 16 accidentés finirent par être opérés. L'opération fut pratiquée chez six d'entre eux dans les 24 heures de l'accident; chez huit autres, on appliqua d'abord un traitement conservateur de quelques jours ou de quelques semaines avant d'opérer. Chez les deux derniers, la lésion diaphragmatique fut réparée respectivement huit mois et quatre ans après la blessure. Lors de l'opération, on découvrit que la rupture diaphragmatique siégeait du côté droit chez trois malades et du côté gauche chez les 13 autres. Dans les cas de lésion droite, le chirurgien eut à résoudre plusieurs difficultés créées par l'anatomie de la région, et dans les cas de déchirure gauche, le contenu abdominal avait dans tous les cas formé une hernie dans l'espace pleural gauche. Les 16 malades ont survécu à l'accident et à l'opération subséquente. Chez 15 malades, n'a persisté aucun défaut pulmonaire. Un des malades se plaint d'être vite fatigué.

RECURRENT PEPTIC ULCERS

The authors evaluated the complications and failures in the treatment of 107 patients with recurrent peptic ulcer after gastroenterostomy, subtotal gastrectomy and vagotomy. Fifty-six patients had been treated initially by partial gastrectomy, 29 by gastrojejunostomy and 22 by vagotomy with either antrectomy, pyloroplasty or gastrojejunostomy.

After one operation for recurrence of an ulcer 57% of the patients had good or excellent results, and after two operations for recurrent ulceration 65% had good results. Vagotomy was the most successful procedure for patients who were initially treated by partial gastrectomy. There were six postoperative deaths, but none occurred in patients treated by vagotomy.

Two groups of patients were particularly difficult to manage—those with recurrent ulceration occurring within one year of the initial procedure and those whose only significant symptom was bleeding. The severity of the ulcer diathesis in these patients often requires aggressive surgical management, including both vagotomy and resection. Of 100 patients who survived one operation for recurrent ulcer, 13 required a third operation, three had confirmed marginal ulcers, which were treated conservatively, and four had upper gastrointestinal hemorrhage.—Jaffe, B. M. *et al.*: Surgical management for recurrent peptic ulcers, *Amer. J. Surg.*, **117:** 214, 1969.

TRAUMATIC ANEURYSM OF THE TEMPORAL ARTERY: A REPORT OF TWO CASES*

CHOSEN LAU, M.D. and G. H. KNUTSON, M.D., F.R.C.S.[C], *Toronto, Ont.*

ANEURYSM of the temporal artery is seldom seen in surgical practice and surgical textbooks pay little or no attention to the subject. In the collected literature, the incidence of temporal artery aneurysms ranges from 0.5% to 2.5% of all aneurysms operated upon. Since the extensive review of Winslow and Edwards[1] (they reported one case and reviewed 107 from the literature up to 1934), sporadic reports, mostly of isolated cases, have appeared in the literature.[2-14] To date, according to our calculations, the English literature contains 114 cases of temporal artery aneurysms and 24 cases of arteriovenous fistulas of this vessel (Table I).[1, 6, 15, 16]

TABLE I.—ANEURYSMS AND ARTERIOVENOUS FISTULAS OF THE TEMPORAL ARTERY REPORTED IN THE ENGLISH LITERATURE

		Temporal artery	
Year	*Author(s)*	*Aneurysms*	*Arteriovenous fistulas*
1932	Tippett[2]	1	—
1935	Winslow and Edwards[1]	93	15
1935	Matas[1]	3	5
1942	Brown and Mehnert[3]	1	—
1944	Bigger[4]	1	—
1947	Perrett[15]	—	1
1949	Smith[5]	1	—
1954	Jahnke, Hughes and Campbell[6]	1	2
1954	Pescovitz and Maloof[7]	1	—
1955	Martin and Shoemaker[8]	1	—
1959	Campbell, Fournier and Hill[9]	2	—
1961	Davies[10]	2	—
1963	Gittes and Kartchner[11]	3	—
1963	Wortzman[12]	1	—
1966	Hite, Groves and Sharkey[13]	1	—
1967	Ferris *et al.*[14]	2	—
1968	Guida and Moore[16]	—	1
	Total	114	24

Recently we encountered two patients with a traumatic aneurysm of the superficial temporal artery; they are the subject of this report.

Case 1.—A 9-year-old girl fell from her bicycle and struck her forehead against a post in early September 1967. A "lump" appeared immediately. We first saw this child six weeks after her injury. On examination she had a 1.5-cm., firm, pulsatile mass on the left, upper forehead covered with bluish overlying skin (Fig. 1). We diagnosed a traumatic aneurysm of the anterior branch of the temporal artery.

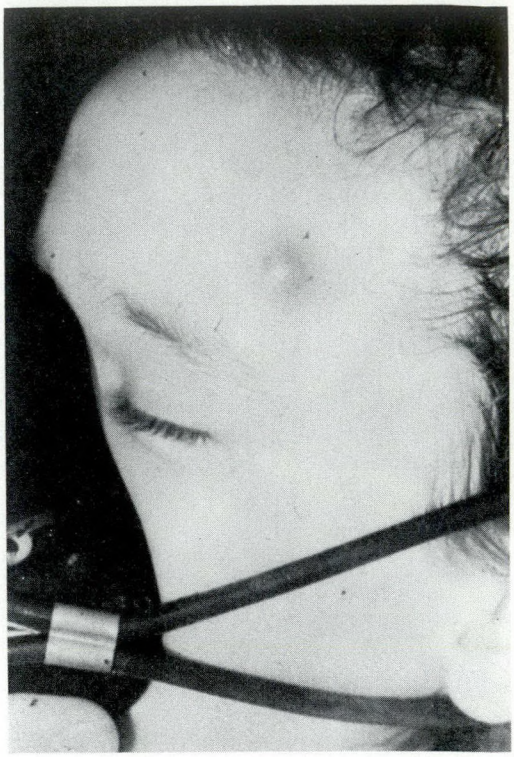

Fig. 1.—Case 1. Traumatic aneurysm of the anterior branch of the temporal artery.

On November 3, 1967, under general anesthesia, the aneurysm was excised through a transverse incision. The feeding vessels were clamped and ligated. Microscopic examination revealed a false aneurysm. The patient's recovery was uneventful.

Case 2.—This 39-year-old white man had been hospitalized for lumbar back pain and a laminectomy was subsequently performed. He was referred to the plastic surgery service because he had an enlarging lump in front of the right ear, which had been present for six months. He recalled being hit by a bottle several weeks before it appeared. A pulsatile mass, 1.8 cm. in diameter, which lay over the course of the superficial temporal artery, suggested the diagnosis of traumatic aneurysm of this artery. On January 31, 1968, under general anesthesia, a fusiform aneurysm of the superficial temporal artery was excised (Fig. 2). His recovery was smooth and he was discharged on February 6.

*From the Department of Plastic Surgery, Toronto Western Hospital, Toronto 130, Ont.

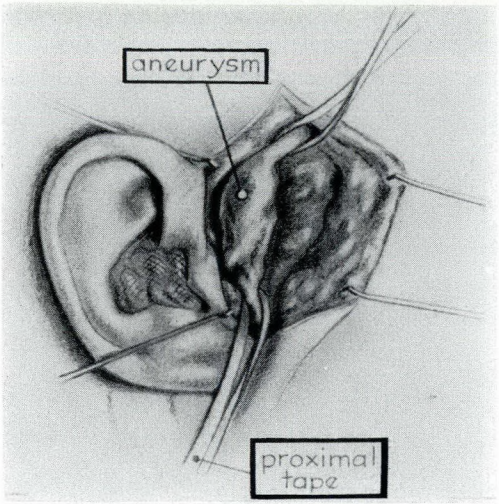

Fig. 2.—Case 2. Excision of a traumatic aneurysm of the temporal artery.

Discussion

The superficial temporal artery arises as a terminal branch of the external carotid behind the neck of the mandible. As it ascends towards the posterior root of the zygoma, it gives off branches to the parotid gland in addition to transverse facial, zygomatic and middle temporal branches. About one inch above the zygoma it ends by dividing into the anterior and posterior branches which run towards the frontal and parietal eminences.

The most common cause of aneurysm of the superficial temporal artery is trauma. The artery and its numerous branches often lie over bone and close to the skin surface where direct trauma may damage the vessel and produce an aneurysm. In Winslow and Edwards' series,[1] 70 out of 108 cases were due to trauma. Spontaneous[3] and arteriosclerotic[8] aneurysms are occasionally reported. In the nineteenth century, blood-letting by arteriotomy for cerebral congestion, meningitis and apoplexy frequently resulted in aneurysm formation. In the early twentieth century, aneurysms were produced by rapier slashes inflicted during student duels in Germany. Puck and hockey-stick injuries in amateur play also produce such aneurysms.[9, 11] In the present era, trauma from vehicle accidents seems to be the leading cause.

The aneurysm is caused by damage to the arterial wall. In blunt trauma, the arterial wall remains intact but, after intramural hemorrhage has weakened the wall, the area is subsequently replaced by fibrous connective tissue. Aneurysmal dilatation follows. The lumen is usually filled with thrombus, which subsequently organizes. In sharp injury, the arterial wall may be partially or completely severed and a false aneurysm may form. When both artery and vein are injured, an arteriovenous fistula can develop.

Previous trauma can usually be elicited in the history. After injury, a mass is usually noted. If the skin is lacerated, bleeding may be profuse and recurrent bleeding may follow on slight provocation. Gradual enlargement of the mass is usual and occasionally there may be associated pulsation and throbbing. Increasing size, disfigurement and throbbing pain bring the victim to the physician.

Because the lesion is superficial, the mass is easily palpable; in size it ranges between 1.5 and 4 cm. Pulsation is easily felt and a bruit is occasionally present. The lesion may decrease in size with proximal compression.

Recently, in four patients, temporal artery aneurysm was recognized before operation by arteriography.[12-14] We do not believe arteriography is necessary for diagnosis but it may be helpful in arteriovenous fistulas.

With the history of trauma and the physical findings, the diagnosis is usually easy. The differential diagnosis lies between sebaceous cyst, lipoma, dermoid cyst,[8] hematoma and abscess.

The treatment of choice is excision of the lesion after proximal and distal ligation. Large aneurysms that may rupture during operation should be controlled by proximal compression before they are excised.

In the cases described in this paper, the patients did not seek, or were not admitted for, a surgical opinion immediately after injury because they had minimal symptoms. In both, the aneurysm was caused by blunt trauma. Injury of the temporal artery is probably more common than is indicated by the few reports in the English literature.

SUMMARY

Two patients had aneurysm of the temporal artery caused by blunt trauma. Neither sought medical advice early because the symptoms were minor. The first, a 9-year-old girl, fell off her bicycle and struck her forehead on a post. She was first seen six weeks after her injury. In the other, a 39-year-old man, the aneurysm was discovered six months later on an admission physical examination. Both aneurysms were excised with good recovery. Injury of the temporal artery probably occurs more often than is indicated by the few reports in the literature. The anatomy, pathology, clinical findings and treatment are briefly reviewed.

REFERENCES

1. WINSLOW, N. AND EDWARDS, M.: Aneurysm of the temporal artery; an analysis of the cases reported in literature to June 1, 1934, and report of a case of traumatic origin, *Amer. J. Surg.*, **28:** 696, 1935.
2. TIPPETT, G. O.: Two cases of traumatic aneurysm, *Brit. Med. J.*, **2:** 711, 1932.
3. BROWN, R. K. AND MEHNERT, R. H.: Aneurysm of the temporal artery; a spontaneous case cured by operation, *Surgery*, **12:** 711, 1942.
4. BIGGER, I. A.: Treatment of traumatic aneurysms and arteriovenous fistulas, *Arch. Surg. (Chicago)*, **49:** 170, 1944.
5. SMITH, F.: A case of traumatic aneurysm of the right superficial temporal artery, *Brit. J. Surg.*, **37:** 241, 1949.
6. JAHNKE, E. J., JR., HUGHES, C. W. AND CAMPBELL, D.: Vascular surgery at Walter Reed Army Hospital. IV. Traumatic arteriovenous fistulas and false aneurysms, *U.S. Armed Forces Med. J.*, **5:** 16, 1954.
7. PESCOVITZ, H. AND MALOOF, W. G.: Aneurysm of the temporal artery due to trauma, *U.S. Armed Forces Med. J.*, **5:** 890, 1954.
8. MARTIN, W. L. AND SHOEMAKER, W. C.: Temporal artery aneurysm, *Amer. J. Surg.*, **89:** 700, 1955.
9. CAMPBELL, J. S., FOURNIER, P. AND HILL, D. P.: Puck aneurysm, *Canad. Med. Ass. J.*, **81:** 922, 1959.
10. DAVIES, D. G.: Traumatic aneurysm of the superficial temporal artery, *Brit. J. Surg.*, **49:** 343, 1961.
11. GITTES, R. F. AND KARTCHNER, M. M.: Post-traumatic temporal artery aneurysm; a recurrent surgical curiosity, *Arch. Surg. (Chicago)*, **87:** 398, 1963.
12. WORTZMAN, G.: Traumatic pseudo-aneurysm of the superficial temporal artery. A case report, *Radiology*, **80:** 444, 1963.
13. HITE, S. J., GROVES, R. A. AND SHARKEY, P. C.: Superficial temporal artery aneurysms, *Neurology (Minneap.)*, **16:** 1044, 1966.
14. FERRIS, E. J. *et al.*: Superficial temporal artery aneurysms, *Radiology*, **88:** 268, 1967.
15. PERRETT, D. G.: Interesting cause of noises in the ear, *Med. J. Aust.*, **1:** 466, 1947.
16. GUIDA, P. M. AND MOORE, S. W.: Aneurysms and arteriovenous fistulas of the temporal artery, *Amer. J. Surg.*, **115:** 825, 1968.

RÉSUMÉ

Nous présentons ici deux cas d'anévrisme de l'artère temporale causé par un traumatisme contondant. Les symptômes étant minimes, les malades tardèrent à consulter le médecin. Une fillette de 9 ans était tombée de son vélo et s'était frappée le front sur un poteau. Or, elle ne fut examinée que six semaines après l'accident. Chez l'autre malade, un homme de 39 ans, l'anévrisme ne fut découvert que six mois plus tard, à l'occasion d'un examen général. On excisa l'anévrisme dans les deux cas et les malades guérirent parfaitement. La lésion de l'artère temporale survient probablement plus souvent que ne semblent vouloir l'indiquer les quelques rapports cités dans la littérature. Les auteurs rappellent brièvement les aspects anatomiques, pathologiques, cliniques et thérapeutiques de cette lésion.

RECANALIZATION OF SYSTEMIC ARTERIAL THROMBI

In 13 dogs, the authors created 14 arterial thromboses, and studied them arteriographically and histologically. They suggest that, unless the lumen of an artery is restored within the first few days, it will not be restored later by any process of recanalization. Two vessels growing into a thrombus have a biological significance that is limited to the thrombus and they play no part in restoring the distal circulation which, in these circumstances, depends upon collateral circulation.

Clot retraction, fibrinolysis, and the disruption and dispersal of thrombus by the force of the circulation may indeed restore a lumen, but this would be expected to occur after blockage. At a late date, the lumen may be enlarged still further by the gradual fibrosis and retraction of the thrombus until it is incorporated in the arterial wall. The idea that blood vessels may slowly infiltrate a thrombus, fuse, and restore the channel is probably fallacious and is not supported by this experimental evidence.—Allison, P. R. and Dunnil, M. S.: Recanalization of systemic arterial thrombi, *J. Cardiovasc. Surg.*, **9:** 383, 1968.

REVIEW ARTICLE

NEUROLOGIC COMPLICATIONS OF OPERATIONS ON THE DESCENDING THORACIC AORTA*

PHILIP T. COLE, M.D.† and JOHN R. GUTELIUS, M.D., F.R.C.S.[C], F.A.C.S.,‡
Montreal, Que.

There is no disease more conducive to clinical humility than aneurysm of the aorta.

William Osler

OSLER made this observation nearly 70 years ago referring to the signs and symptoms of aortic aneurysms and their frequent precursor—syphilis. Today, with refined diagnostic methods, surgeons are unlikely to be embarrassed because they cannot detect aneurysm formation. However, if we turn from diagnosis to treatment, particularly treatment of an aneurysm within the thorax, Osler's words remain appropriate. We recently reported a patient in whom replacement of the descending thoracic aorta was followed by paraplegia of obscure origin and death.[1] A survey of the literature on this complication showed only a moderate body of widely scattered knowledge; no comprehensive review of this subject has been made for more than 10 years. This is surprising because aneurysm of the descending thoracic aorta, the most common intrathoracic aneurysm,[2] is resected in many centres. This survey also suggests that one technique still used during such procedures, namely, the use of the left subclavian artery to bypass the occluded aorta, may itself contribute to these neurologic complications. For these reasons we reviewed the literature.

Aortic aneurysm has always been viewed as a dangerous and frequently fatal lesion, especially when the thoracic aorta is involved; such involvement suggested syphilis and a rapidly progressive course.[3] In 1952 Cooley and DeBakey[4] estimated that, at diagnosis, the average patient with a thoracic aneurysm had only six to eight months to live. Ten years later Creech[5] made a similar estimate. In 1964 Joyce *et al.*,[6] reviewing the prognosis of non-surgically treated aneurysms of the thoracic aorta, found that 50% of these patients survived for five years while 90% of controls survived for this period. The 10-year survivals were 30% and 78% respectively. These more optimistic figures suggest that fewer lesions are now syphilitic, that non-surgical treatment has improved and that the lesions are now diagnosed earlier. Joyce *et al.* also assessed guides to prognosis for the untreated lesion and came to the following conclusions: the shape and location of the aneurysm and the sex of the patient have no prognostic value. If the patient is over 50 years old, if he has diastolic hypertension or other cardiovascular disease or if the aneurysm is more than 6 cm. wide, his survival is shortened. If the patient has other arteriosclerotic disease or if the aneurysm produces signs or symptoms, the prognosis is extremely poor. As for surgically treated aneurysms, DeBakey *et al.*[2] have shown that overall hospital mortality can be kept below 20%; in patients over 60, however, an operative mortality of 45% may be expected. Kirklin[3] suggested that these older patients be observed to see if the aneurysm is enlarging.

The surgeon must be aware of the natural history of the disease and its operative mortality; in addition, his decision to operate on the thoracic aorta should be taken in the light of the complications that may result. He understands the basis for most of these, such as hemorrhage, infection, phrenic and recurrent nerve palsy and can take steps to prevent them; however, the most tragic and least understood of these complications are neurologic.[7-9] The incidence of neurologic complications after operations on the thoracic aorta is un-

*From the Department of Surgery, McGill University, and Royal Victoria Hospital, Montreal, Que.

†Former Intern, Department of Surgery, Royal Victoria Hospital. Present address: Harvard School of Public Health, 665 Huntington Avenue, Boston, Mass. 02115, U.S.A.

‡Associate Professor of Surgery, McGill University. Markle Scholar in Academic Medicine.

known but may be as high as 6%,[2, 10] in contrast to their extreme rarity after operations on the abdominal aorta.[11, 12]

The earliest studies of aortic lesions dealt with coarctation in animals; in coarctation extensive collateral circulation is usually present. Aneurysm, however, provides little or no stimulus to the development of collaterals except if the intercostal vessels are obliterated by atheromata or mural thrombi.[13] This absence of collateral circulation was recognized early and it was understood that obliterative surgical techniques that did not re-establish aortic flow would rarely succeed. Herein lies the dilemma: in order to re-establish flow, the surgeon must remove the diseased segment from the circulation but, in so doing, he may also remove the source of blood flow to vital radicular arteries. Because of this dilemma, surgical treatment of aortic aneurysms was confined for years to attempts to slow the enlargement by inducing thrombosis within the sac or provoking mural fibrosis.[14]

Early attempts to resect intrathoracic aneurysms were uniformly unsuccessful, but during the 1940's several successful aneurysmectomies were performed.[15-17] However, the goal of aneurysm surgery, total excision and replacement, was not realized in a thoracic lesion until 1951. In that year Lam and Aram,[18] operating on a 56-year-old man, replaced a segment of the descending thoracic aorta with a homograft. After operation the patient was paraplegic and, because of suture-line disruption, died 11 weeks later. In the next few years many surgeons demonstrated that it was feasible to replace the thoracic aorta.[14, 19-24]

Replacement of a segment of the descending thoracic aorta poses two distinct threats to the integrity of the spinal cord: first, the surgeon must interrupt aortic flow temporarily thus inducing distal hypoxia; this difficulty is usually overcome by shunting procedures. Second, in removing the aortic segment, the surgeon may also remove a vital part of the blood supply to the cord. This second possibility is now the principal concern in these procedures. Certain factors contribute to both difficulties and the most important of these, the anatomy of the spinal cord blood supply, will be considered in detail.

Spinal Cord Blood Supply

The spinal cord has two blood supplies: a continuous system and a segmental system. Adams and van Geertruyden[25] showed that, with respect to blood supply, most cords fall into one of two groups: Group 1 (primarily continuous) are those with a large and high great radicular artery associated with a well-developed anterior spinal artery but with few radicular arteries. Group 2 (primarily segmental) is comprised of cords with a lower and smaller great radicular artery associated with a less developed anterior spinal artery. However, this type has a greater number of radicular arteries. Although individuals are divided almost equally between these two groups (all have both segmental and continuous blood supplies), one system usually predominates.[25]

The simpler continuous system (Fig. 1A) includes only three vessels—the anterior spinal artery and two posterior spinal arteries. The anterior spinal artery commonly

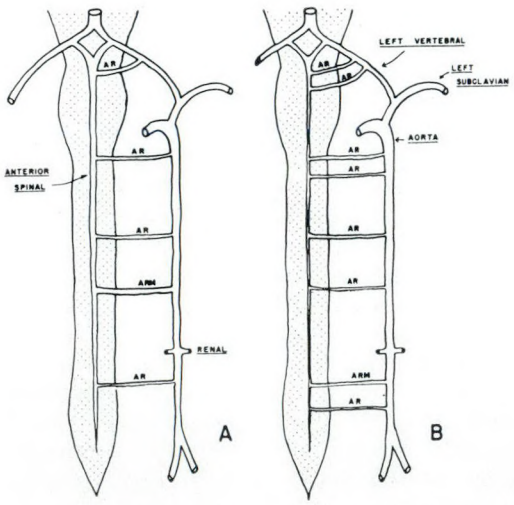

Fig. 1.—Schematic representation of the spinal blood supply. (A) The continuous system predominates with a well-developed anterior spinal artery, few radicular arteries (AR) a high great radicular artery (ARM) and, not shown, two substantial posterior spinal arteries. (B) The segmental system predominates with many radicular arteries and a low great radicular artery. The anterior spinal artery and the posterior spinal arteries are narrow and may be discontinuous.

originates on the anterior surface of the cervical cord from anastomosis of branches from the left and right vertebrals. In up to 10% of humans the right or left contributing branch is insignificant and the anterior spinal artery originates unilaterally.[26, 27] In the cervical region the anterior spinal artery usually receives one or two more "segmental" vessels from the ascending cervical or the vertebral artery of either side.[28, 29] It then descends on the anterior surface of the cord and is largest in the lumbar and upper cervical regions and smallest in the upper thoracic region. The vessel may become quite small but is almost always continuous to the filum terminale.[28, 30] The anterior spinal artery supplies at least 75% of the cord, failing to reach only the dorsal columns and part of the posterior horns.[31, 32] Thus, when paraplegia follows an aortic operation, the dorsal column is usually preserved, but the anterior sensory functions are lost.[32-34] The other important components of the continuous system are the paired posterior spinal arteries lying in the posterolateral sulci of the cord. These arise from the posterior inferior cerebellar or the vertebral arteries.[28] The posterior spinal arteries may receive some segmental contribution from cervical branches of the vertebrals, but thereafter derive their only important source of blood from anastomoses with the anterior spinal artery.[28, 31, 34] The posterior spinal arteries provide 25% or less of the blood to the cord and may be small or discontinuous.[29]

The second principal blood supply to the cord is the segmental system (Fig. 1B) which is composed of the anterior spinal branches of the intercostal and lumbar arteries, the radicular arteries. There are usually 17 pairs of radicular arteries but only about one-quarter of their anterior spinal branches ultimately supply blood to the cord. They do so by contributing to the anterior spinal artery.[29, 31, 35] Including the branches of the vertebrals and the ascending cervical arteries, usually five to eight segmental vessels supply the cord. (The branches received in the neck are not actually segmental vessels but are analogous and conveniently considered as such.) Of these, two to four are cervical, one or two are upper thoracic, none or one midthoracic and one may be lower thoracic. There are also one or two in the lumbar region.[29] All the anterior spinal branches are important but in most individuals one, the great radicular artery (arteria radicularis magna), is larger and more important than the others[25] and deserves special attention. This vessel may be found at any level from T6 to L5 but usually is on the left at L2.[29, 30, 36]

Although the spinal cord blood supply has been divided into two systems for the sake of description, these systems are inseparable. They are united by the anterior spinal artery, which may be thought of as a continuous vessel formed by the joining together of the ascending and descending branches of each successive anterior segmental artery.

It has been suggested that the middle and lower thoracic regions of the cord are poorly vascularized and this is true if one considers vessels per inch of aorta. The surgeon of course views the situation exactly this way. He is concerned with the length of aorta mobilized and the number of radicular arteries ligated during any given procedure. However, the blood supply to the cord at any level is proportional to the cell population at that level.[30] The vascular supply of the thoracic cord looks poor because the thoracic segments are much longer than those of other regions.[25] Many writers speak of the cord's "poor" or "inadequate" blood supply which is erroneous because the spinal cord, like other central nervous system tissue, is richly supplied with blood.[36] However, this supply is tenuous because a few vessels serve a great length of tissue and anastomoses are infrequent. The spinal cord, then, is a segmental, elongated structure which is provided with an abundant but precarious blood supply. However, beyond these anatomic considerations the surgeon must realize that this is a connected system of vessels ranging from the upper reaches of the vertebrals to the filum terminale; with changing circumstances, the pressure, rate and even direction of blood flow may change within the system. This may result from transient changes such as alteration in body position or, of course,

from aortic cross-clamping. These changes may also be brought about by relatively permanent alterations such as atherosclerosis, the development of collateral circulation and, of special interest, the operative sacrifice of vessels supplying the cord. In keeping with these concepts of temporary and permanent changes in spinal blood flow, we shall review the literature in two sections: that dealing with aortic occlusion and that dealing with resection.

Aortic Occlusion

When the thoracic aorta is clamped, proximal hypertension and left ventricular strain develop immediately. The heart fails and the patient may die from pulmonary edema or cerebral damage. Immediate distal hypotension also develops with ischemia of the liver, gastrointestinal tract, kidneys, peripheral nerves and other tissues. However, the tissue most vital is the spinal cord, because this structure is least resistant to hypoxia.[8, 25] Some of the factors affecting the incidence and severity of spinal cord ischemia are as follows: age—younger patients have a greater potential collateral circulation; cardiac output—the extent to which a collateral circulation has already developed; and the level and duration of the occlusion.[25, 37] However, the most important factors are the individual pattern of spinal cord blood supply and the specific measures the surgeon has taken to protect the cord.[34, 37] These measures include numerous shunting techniques, hypothermia and, experimentally, the draining off of the cerebrospinal fluid (CSF).

The intraluminal shunt, the first type to be used with success, temporarily replaces the lumen of the segment to be resected. This, however, is difficult to manipulate and can be used only when the diseased segment is short and the aorta above and below is nearly normal.[34] However, intraluminal shunts have several advantages: anticoagulants are eliminated and the surgeon saves time because he does not have to make temporary anastomoses or secondary dissections for extraluminal shunts. Though rarely employed today, intraluminal shunts are still useful if the lesion is suitable.[38]

Intraluminal shunts were largely discarded, not because of difficulties associated with their use, but because hypothermia was introduced. In animals, lowering of body temperature protected the spinal cord against infarction, but did not improve overall survival.[39, 40] In man, this technique protected the spinal cord better than did the intraluminal shunt. However, hypothermia was also discarded after a brief period, for several reasons; it aggravated the tendency to cardiac fibrillation, caused aberrations of the clotting mechanism, predisposed to metabolic acidosis and increased pulmonary complications.[8] In addition, hypothermia and postoperative rewarming of the patient are time consuming and cumbersome. Furthermore, even with hypothermia, as many as one-half of those who undergo aortic resection may have at least transient sequelae.[25] In 1963 Braimbridge,[37] after reviewing the literature, showed that, although hypothermia decreased paraplegia, the overall mortality with this technique was greater than when other methods were used to protect the aorta.

In the search for better protection of the spinal cord, extraluminal shunts were developed. The prototypes—long, narrow tubes—met with little success;[41] because of high resistance, they transported inadequate volumes of blood. Eventually, shorter and wider shunts were developed. The surgeon sews the extraluminal shunt end-to-side to the aorta above and below the segment to be resected and, after blood flow is established through the shunt, he resects the aneurysm. These shunts are difficult to fix in place, occupy much space in the operating field,[34] and the operator has no way of assessing or controlling the blood flow through them.[8] Even if they function well, there may be distal hypoxia and when flow is restored in the main channel the patient remains hypotensive because the peripheral resistance is inadequate.[42] In spite of these disadvantages, extraluminal shunts were brought to a high degree of refinement and are still used occasionally.

Currently, the most popular method for circumventing the clamped aorta is the "remote" extraluminal shunt. The inflow to

this shunt may come from any of the cardiac chambers, the left subclavian artery or either femoral vein, but the left atrium and the left subclavian artery are most commonly used.[3, 19, 37, 43] Either femoral artery is used for distal return. These shunts are easy to place and are outside the operative field. The flow in remote shunts is usually augmented by a pump or pump oxygenator and, by this means, the flow can be regulated. The most recent development uses a femoral vein to femoral artery shunt augmented by a pump oxygenator. The proponents of this shunt claim three principal advantages: it is entirely removed from the operative field; it can be established while the thoracotomy is being done, thus saving time; and it does not require the nearly constant balance between cardiac output and femoral artery return as do those using a source above the proximal aortic clamp.[44] If this new procedure works as well for others as for its developers, it will probably be our best approach to the prevention of spinal cord ischemia after aortic occlusion.

When they evaluated extraluminal shunts, Austen and Shaw[45] found that one can usually avoid right-heart bypass and the necessity for complex equipment and trained technicians, and thereby minimize the priming volume and the risk of air emboli. In advocating left-heart bypass only, they concluded that both the left atrium and the left subclavian artery were suitable for inflow and that the "source most readily available in the operative field should be used".[45]

One other procedure, drainage of the CSF before clamping, has been used with success in animals to prevent spinal cord ischemia during aortic occlusion and resection and, because of its possible future application in man, will be briefly described here. In 1939 Van Harreveld and Marmont[46] made the spinal cord of dogs ischemic by raising pressure within the vertebral canal higher than the blood pressure. In 1960 Miyamoto *et al.*[47] showed that when the thoracic aorta is clamped, the CSF pressure rises immediately. Knowing about Van Harreveld's early work, they suspected that this rise could cause poor spinal cord perfusion. By draining the CSF before the aorta was clamped, these workers prevented both the rise in CSF pressure and neurologic deficits in dogs. In 1962 Blaisdell and Cooley[7] confirmed this work and concluded that, if the CSF pressure equalled or exceeded distal aortic pressure during the period of occlusion, paraplegia or death was inevitable. They suggested that low CSF pressure allowed a sufficient pressure gradient to develop between aortic branches and segmental vessels so that blood flowed into the cord despite low aortic pressure.[31, 48, 49]

Aortic Resection

Even when aortic occlusion has been compensated for by shunting, the spinal cord may infarct because critical sources of blood were sacrificed when the aortic segment was excised. In this context Eiseman[35] pointed out that the number and level of vessels destroyed during aortic resection are just as important as the period of occlusion.[50]

Most of our knowledge about the difficulties associated with aortic resection are derived from experiments on the dog. We must, however, be wary of extrapolating these results to man because there are several major differences in the spinal cord and its blood supply in these species.[51] The dog can tolerate without neurologic deficit the ligation of all intercostal arteries arising from the aorta.[7, 13, 18, 52] If the left subclavian artery is also ligated, 85% of dogs will have a neurologic deficit.[52] However, Spencer and Zimmerman[13] showed that if any two pairs of intercostal arteries were spared, the frequency of paraplegia was very low. Killen and Adkins[9] showed further that any two pairs of intercostal arteries maintained the "mean parietal pressure" (an approximation of the blood pressure within the anterior spinal artery) at about 60 mm. Hg. Also, a mean parietal pressure of 30 mm. Hg could be considered "critical" because below this level 90% of dogs developed a neurologic deficit whereas above this level paraplegia did not occur. It is of possibly greater significance that, after ligation of the intercostal vessels, mean parietal pressure rose by 17 to 38 mm. Hg during a four-hour period. This rise suggests that a potential collateral circulation

was being "opened up". If this experiment can be reproduced in man, it suggests that, if the spinal cord can be "carried over" for four hours, enough circulation might develop to maintain viability.

Edwards and Killen[53] sacrificed vital spinal cord vessels using a two-stage procedure. They tied off the eight highest intercostal arteries one day and the remaining vessels on the following day. This delay reduced the frequency of neurologic deficit from 70% to 50%. However, if the two operations were done one week apart, the incidence was zero. In this experiment, done in healthy dogs, the low-lying great radicular artery was always spared.

Spencer and Zimmerman[13] took another approach to aortic resection, removing an ellipse (including the orifice of one or two patent intercostal vessels) from the segment to be replaced. This ellipse was sutured to the prosthetic aorta in the hope that intercostal circulation would be restored. Because of technical difficulties, this procedure cannot be done in man; furthermore, the surgeon would not know which intercostals were important to a particular patient.

During aortic occlusion, the problems encountered are related to the level of clamping. However, our understanding of the blood supply to the spinal cord suggests that, when the aorta is excised, the segments removed are more critical than the level or duration of occlusion. As Adams and van Geertruyden[25] pointed out, in patients in their Group 1 (high great radicular artery, well-developed anterior spinal artery but poor segmental supply), operations on the distal two-thirds of the descending aorta are more dangerous than those above this level. In the first procedure, the surgeon may ligate an intrathoracic great radicular artery and cause infarction of the spinal cord or the medulla oblongata. On this point these authors state that a lesion in the lower thoracic aorta can be resected safely only if the great radicular artery arises from the abdominal aorta. This will be the case in only approximately 50% of cases. Obviously we would be in a better position if we could delineate the blood supply to the cord by preoperative angiography. Then we could recommend resection to patients who had a lumbar great radicular artery. For patients with an intrathoracic great radicular artery close to the aneurysm, a conservative approach could be adopted for all but the largest or most rapidly advancing vascular lesions. Unfortunately, such precise radiographic delineation has not been practical because of technical problems and because available contrast media are not well tolerated by the cord.[54, 55] However, Doppman and Di Chiro[56] recently described 10 patients in whom the great radicular artery was delinated radiographically without complication. However, until this procedure is proved safe and is generally available, we have no adequate means of recognizing those patients most susceptible to the neurologic sequelae of aortic resection.

Conclusions

Although the vessels supplying the cord are important, there are three reasons for believing that, like the great radicular artery, the left subclavian-vertebral artery complex is particularly important and that its function should be maintained during aortic occlusion and after resection.

First, Adams and van Geertruyden[25] showed that, if there was no high thoracic radicular artery, the subclavian arteries could supply the entire upper one-half of the cord. However, they also wrote "(when the left subclavian artery is sacrificed) . . . only the occlusion of the costocervical trunk is of concern as the left vertebral has a good collateral circulation via the basilar". They could not, of course, take into account the "subclavian steal syndrome" described five years later. They believed that, even if the left subclavian artery was sacrificed, the anterior spinal artery would still be filled by a well-supplied vertebral—an assumption that is no longer tenable because we now know that, in some cases, this blood would be shunted to the arm.[26]

Second, in 1959 Thomas *et al.*[27] showed that, when the left vertebral artery is sacrificed, up to 9% of patients may develop basilar artery insufficiency because flow in the right vertebral is inadequate. In 1960 Jones *et al.*[57] described a series of patients in whom the left vertebral was ligated

when the left subclavian artery was used as a shunt source; 6% of them developed basilar artery insufficiency and died.

Much of this information was brought together by Reivich *et al.*[26] These workers pointed out that brain stem ischemia could result from stenosis of a subclavian artery proximal to the vertebral takeoff. The now well-recognized subclavian steal syndrome provides a third reason to avoid cannulation of the left subclavian artery. Such a cannula could induce an "iatrogenic subclavian steal" during the time when spinal blood flow was marginal. Not

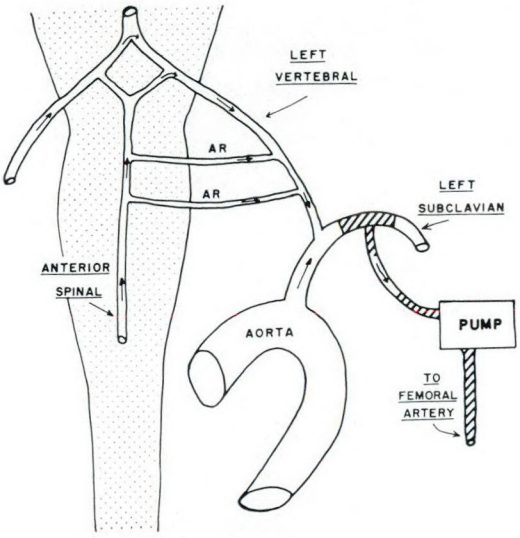

Fig. 2.—The left subclavian artery as a shunt source. This arrangement may create an "iatrogenic subclavian steal" possibly reversing blood flow in the anterior spinal artery.

only would such a cannula reduce blood flow in the left vertebral artery and its cord branches, but Schechter and Zingesser[58] suggested that, under such circumstances, flow in the anterior spinal artery actually reverses and blood travels away from the cord to the brain stem and the vertebral arteries. Such poor or even reversed flow in the cephalad regions of the cord may be detrimental to the precariously supplied thoracic and lumbar regions (Fig. 2). Furthermore, when the left subclavian artery is used to make a shunt, it may be necessary to transect the vertebral to gain access to it. On the other hand, when the shunt is removed the left subclavian artery with or without its vertebral branch is usually ligated rather than repaired; then the left vertebral artery can no longer provide blood to the brain stem and spinal cord.

Before sacrificing the left subclavian artery Reivich *et al.*[26] recommended that the surgeon study the aortic arch to evaluate the adequacy of the right vertebral artery which would have to supply most of the blood to the basilar and the anterior spinal arteries. Others have suggested right vertebral angiography under the same circumstances.[27] Reivich *et al.* also suggested that, when the left subclavian artery must be ligated, this be done distal to the vertebral origin. However, if the ligature must be placed proximal to the vertebral, then the surgeon should perhaps ligate the vertebral in order to prevent a subclavian steal syndrome. However, this should be done only when the right vertebral is adequate.

In view of the possible sequelae and because the left atrium, a more desirable shunt source, is usually readily available, we suggest that the left subclavian artery should not be used to provide a shunt when resecting an aortic aneurysm.

References

1. Cole, P. T. and Gutelius, J. R.: Paraplegia resulting from the use of the subclavian artery as a shunt source during resection of the descending thoracic aorta, *Ann. Surg.*, **169:** 293, 1969.
2. DeBakey, M. E. *et al.*: Aneurysms of the thoracic aorta. Analysis of 179 patients treated by resection, *J. Thorac. Surg.*, **36:** 393, 1958.
3. Kirklin, J. W.: Surgical treatment of aneurysms. *In*: Peripheral vascular disease, 3rd ed., edited by E. V. Allen, N. W. Barker and E. A. Hines, W. B. Saunders Company, Philadelphia, 1962, p. 883.
4. Cooley, D. A. and DeBakey, M. E.: Surgical considerations of intrathoracic aneurysms of the aorta and great vessels, *Ann. Surg.*, **135:** 660, 1952.
5. Creech, O., Jr.: Thoracic aneurysms. *In:* Surgical treatment of peripheral vascular disease, edited by W. F. Barker, McGraw-Hill Book Company, New York, 1962, p. 269.
6. Joyce, J. W. *et al.*: Aneurysm of the thoracic aorta. A clinical study with special reference to prognosis, *Circulation*, **29:** 176, 1964.
7. Blaisdell, F. W. and Cooley, D. A.: The mechanism of paraplegia after temporary thoracic aortic occlusion and its relationship to spinal fluid pressure, *Surgery*, **51:** 351, 1962.

8. Cooley, D. A., DeBakey, M. E. and Morris, G. C., Jr.: Controlled extracorporeal circulation in surgical treatment of aortic aneurysm, *Ann. Surg.*, **146:** 473, 1957.
9. Killen, D. A. and Adkins, R. B., Jr.: Studies of spinal arterial bed pressure following extensive mobilization of the aorta from the posterior parietes, *J. Thorac. Cardiovasc. Surg.*, **49:** 231, 1965.
10. Ellis, F. H., Jr., Kirklin, J. W. and Bruwer, A. J.: Surgical experiences in the treatment of aneurysms of the thoracic aorta, *Surg. Gynec. Obstet.*, **106:** 179, 1958.
11. Hara, M. and Lipin, R.: Spinal cord injury following resection of abdominal aortic aneurysm, *A.M.A. Arch. Surg.*, **80:** 419, 1960.
12. Sheranian, L. O., Edwards, J. E. and Kirklin, J. W.: Late results in 110 patients with abdominal aortic aneurysm treated by resectional placement of aortic homograft, *Surg. Gynec. Obstet.*, **109:** 309, 1959.
13. Spencer, F. C. and Zimmerman, J. M.: The influence of ligation of intercostal arteries on paraplegia in dogs, *Surg. Forum*, **9:** 340, 1958.
14. Cooley, D. A. and De Bakey, M. E.: Resection of entire ascending aorta in fusiform aneurysm using cardiac bypass, *J. A. M. A.*, **162:** 1158, 1956.
15. Alexander, J. and Byron, F. X.: Aortectomy for thoracic aneurysm, *J. A. M. A.*, **126:** 1139, 1944.
16. Monod, O. and Meyer, A.: Resection of an aneurysm of the arch of the aorta with preservation of the lumen of the vessel, *Circulation*, **1:** 220, 1950.
17. Ochsner, A.: Personal communication: cited by Creech. O., Jr.: Thoracic aneurysms. *In:* Surgical treatment of peripheral vascular disease, edited by W. F. Barker. McGraw-Hill Book Company, New York, 1962, p. 269.
18. Lam, C. R. and Aram, H. H.: Resection of the descending thoracic aorta for aneurysm; report of the use of the homograft in case and experimental study, *Ann. Surg.*, **134:** 743, 1951.
19. Cooley, D. A., Mahaffey, D. E. and De Bakey, M. E.: Total excision of the aortic arch for aneurysm, *Surg. Gynec. Obstet.*, **101:** 667, 1955.
20. Creech, O., Jr., De Bakey, M. E. and Mahaffey, D. E.: Total resection of the aortic arch, *Surgery*, **40:** 817, 1956.
21. De Bakey, M. E. and Cooley, D. A.: Successful resection of aneurysm of thoracic aorta and replacement by graft, *J. A. M. A.*, **152:** 673, 1953.
22. De Bakey, M. E. and Cooley, D. A.: Successful resection of aneurysm of distal aortic arch and replacement by graft, *J. A. M. A.*, **155:** 1398, 1954.
23. De Bakey, M. E. *et al.*: Successful resection of fusiform aneurysm of aortic arch with replacement by homograft, *Surg. Gynec. Obstet.*, **105:** 657, 1957.
24. Stranahan, A. *et al.*: Aortic arch resection and grafting for aneurysm employing an external shunt, *J. Thorac. Surg.*, **29:** 54, 1955.
25. Adams, H. D. and van Geertruyden, H. H.: Neurologic complications of aortic surgery, *Ann. Surg.*, **144:** 574, 1956.
26. Reivich, M. *et al.*: Reversal of blood flow through the vertebral artery and its effect on cerebral circulation, *New Eng. J. Med.*, **265:** 878, 1961.
27. Thomas, G. I. *et al.*: The significance of anomalous vertebral-basilar artery communications in operations on the heart and great vessels: an illustrative case with review of the literature, *Surgery*, **46:** 747, 1959.
28. Gray, H.: Anatomy of the human body, 27th ed., edited by C. M. Goss, Lea & Febiger, Philadelphia, 1959.
29. Suh, T. H. and Alexander, L.: Vascular system of the human spinal cord, *Arch. Neurol. Psychiat. (Chicago)*, **41:** 659, 1939.
30. Gillilan, L. A.: The arterial blood supply of the human spinal cord, *J. Comp. Neurol.*, **110:** 75, 1958.
31. Bolton, B.: The blood supply of the human spinal cord, *J. Neurol. Psychiat.*, **2:** 137, 1939.
32. Mehrez, I. O. *et al.*: Paraplegia following resection of abdominal aortic aneurysm, *Ann. Surg.*, **156:** 890, 1962.
33. Beattie, E. J., Jr., Nolan, J. J. and Howe, J. S.: Paralysis following surgical correction of coarctation of the aorta; a case report with autopsy findings, *Surgery*, **33:** 754, 1953.
34. Cooley, D. A.: Complications of procedures on the thoracic aorta. *In:* Complications in surgery and their management, edited by C. P. Artz and J. D. Hardy, W. B. Saunders Company, Philadelphia, 1960, p. 511.
35. Eiseman, B. and Summers, W. B.: Factors affecting spinal cord ischemia during aortic occlusion, *Surgery*, **38:** 1063, 1955.
36. Lazorthes, G. *et al.*: La vascularisation artérielle de la moelle; recherches anatomiques et applications à la pathologie médullaire et à la pathologie aortique, *Neurochirurgie*, **4:** 3, 1958.
37. Braimbridge, M. V.: Surgery of the descending thoracic aorta, *Ann. Roy. Coll. Surg. Eng.*, **33:** 344, 1963.
38. Keon, W. J. and Trimble, A. S.: Thoracic aneurysm: a simplified method of resection, *J. Thorac. Cardiovasc. Surg.*, **56:** 408, 1968.
39. Owens, J. C., Prevedel, A. E. and Swan, H.: Prolonged experimental occlusion of thoracic aorta during hypothermia, *A.M.A. Arch. Surg.*, **70:** 95, 1955.
40. Pontius, R. G. *et al.*: The use of hypothermia in the prevention of paraplegia following temporary aortic occlusion: experimental observations. *Surgery*, **36:** 33, 1954.
41. Schafer, P. W. and Hardin, C. A.: The use of temporary polythene shunts to permit occlusion, resection and frozen homologous graft replacement of vital vessel segments; a laboratory and clinical study, *Surgery*, **31:** 186, 1952.
42. Ellison, R. G., Cope, J. A. and Moretz, W. H.: Technical problems in the surgical repair of intrathoracic aneurysms. *J. Thorac. Cardiovasc. Surg.*, **39:** 486, 1960.
43. Groves, L. K.: Experience with thirteen cases of resection of aneurysms of the descending thoracic aorta, *Cleveland Clin. Quart.*, **28:** 176, 1961.
44. Neville, W. E. *et al.*: Resection of the descending thoracic aorta with femoral vein to femoral artery oxygenation perfusion, *J. Thorac. Cardiovasc. Surg.*, **56:** 39, 1968.

45. Austen, W. G. and Shaw, R. S.: Experimental studies with extracorporeal circuits as a method to enable surgical attack on thoracic aneurysms, *J. Thorac. Cardiovasc. Surg.*, **39:** 337, 1960.
46. Van Harreveld, A. and Marmont, G.: The course of recovery of the spinal cord from asphyxia, *J. Neurophysiol.*, **2:** 101, 1939.
47. Miyamoto, K. *et al.*: A new and simple method of preventing spinal cord damage following temporary occlusion of the thoracic aorta by draining the cerebrospinal fluid, *J. Cardiovasc. Surg. (Torino)*, **1:** 188, 1960.
48. Killen, D. A. *et al.*: Effect of low molecular weight dextran, heparin, urea, cerebrospinal fluid drainage and hypothermia on ischemic injury of the spinal cord secondary to mobilization of the thoracic aorta from the posterior parietes, *J. Thorac. Cardiovasc. Surg.*, **50:** 882, 1965.
49. Mercati, U. *et al.*: Utilità dell'ipotensione liquorale per la prevenzione dei danni ischemici midollari secondari a clampaggio dell'aorta toracica alta. Studio spermentale, *Gazz. Int. Med. Chir.*, **69:** 2369, 1964.
50. Parkins, W. M., Ben, M. and Vars, H. M.: Tolerance of temporary occlusion of the thoracic aorta in normothermic and hypothermic dogs, *Surgery*, **38:** 38, 1955.
51. Giuseffi, J., Greene, L. W., Jr. and Vetto, M.: Experiments on occlusion of the abdominal aorta in normothermic dogs, *Surg. Gynec. Obstet.*, **105:** 427, 1957.
52. Killen, D. A. *et al.*: Spinal cord ischemia following mobilization of canine aorta from posterior parietes, *Ann. Surg.*, **162:** 1063, 1965.
53. Edwards, R. H. and Killen, D. A.: Prevention of spinal cord ischemia incident to extensive mobilization of the thoracic aorta from the posterior parietes, *Surg. Forum*, **15:** 285, 1964.
54. Efsen, F.: Spinal cord lesion as a complication of abdominal aortography. Report of 4 cases, *Acta Radiol. [Diagn.] (Stockholm)*, **4:** 47, 1966.
55. Tarazi, A. K., Margolis, G. and Grimson, K. S.: Spinal cord lesions produced by aortography in dogs, *A.M.A. Arch. Surg.*, **72:** 38, 1956.
56. Doppman, J. and Di Chiro, G.: The arteria radicularis magna: radiographic anatomy in the adult, *Brit. J. Radiol.*, **41:** 40, 1968.
57. Jones, T. W. *et al.*: Arterial complications incident to cannulation in open-heart surgery with special reference to the femoral artery, *Ann. Surg.*, **152:** 969, 1960.
58. Schechter, M. M. and Zingesser, L. H.: The anterior spinal artery, *Acta Radiol. [Diagn.] (Stockholm)*, **3:** 489, 1965.

Résumé

L'article expose brièvement l'historique et les considérations fondamentales de la chirurgie des branches diaphragmatiques des artères médiastinales. Pour éviter les complications neurologiques, il faut bien comprendre et la vascularisation de la moelle épinière et les techniques actuelles destinées à la sauvegarder. Ces points sont exposés en détail. On attire l'attention sur deux risques possibles. Le premier, soit l'occlusion de l'aorte, peut être généralement corrigé par une dérivation et par d'autres techniques intra-opératoires. Mais si l'occlusion est bien tolérée, il n'en demeure pas moins qu'un infarctus de la moelle épinière peut résulter du sacrifice de vaisseaux qui ont un rôle vital pour la moelle. Ce second problème ne peut être évité ou réduit au minimum que par une parfaite connaissance de l'anatomie de la vascularisation de la moelle épinière. Enfin, les auteurs croient que l'artère sous-clavière gauche est à rejeter comme source d'une dérivation, tant au point anatomique que sur le plan hémodynamique.

CASE REPORTS

MALIGNANT MESENCHYMOMA OF THE MANDIBLE*

E. E. STERNS, M.D., F.R.C.S.[C], F.A.C.S.,† M. DARIA HAUST, M.D., M.Sc.(Med.)‡ and D. G. WOLLIN, M.D.,§ *Kingston, Ont.*

In 1948 Stout[1] described eight patients with malignant tumours arising from several mesenchymal elements. Although he was not the first to coin the term "mesenchymoma", he advocated that it be confined to a group of rare tumours, benign and malignant, that arise from two or more elements of mesenchyme not including fibrous tissue. These tumours, which may be composed of vascular elements, cartilage, bone, fat, smooth and striated muscle and myxomatous material, have been found in all areas of the body.

Only two malignant mesenchymomas arising from bone have been reported to date. In 1959 Kipkie and Haust[2] described a patient with a malignant mesenchymoma of the mandible. The other osseous mesenchymoma, which arose in the tibia, was reported by Schajowicz, Cuevillas and Silberman.[3]

In this communication we wish to describe a 15-year-old boy with a malignant mesenchymoma of the mandible.

Case Report

On January 24, 1966, R.T., a 15-year-old Caucasian boy, was admitted to the Kingston General Hospital because of a rapidly expanding lesion of the chin. He had been in good health until three weeks before when his mother noted a swelling over the symphysis of the mandible. From a barely detectable mass, it grew rapidly but painlessly. It was thought to be inflammatory but did not respond to penicillin, and attempted drainage by the family physician yielded no pus. Radiographs taken on January 19, five days before the first admission to hospital, showed localized destruction in the central portion of the body of the mandible with spicules radiating anteriorly into the soft tissue (Fig. 1). A

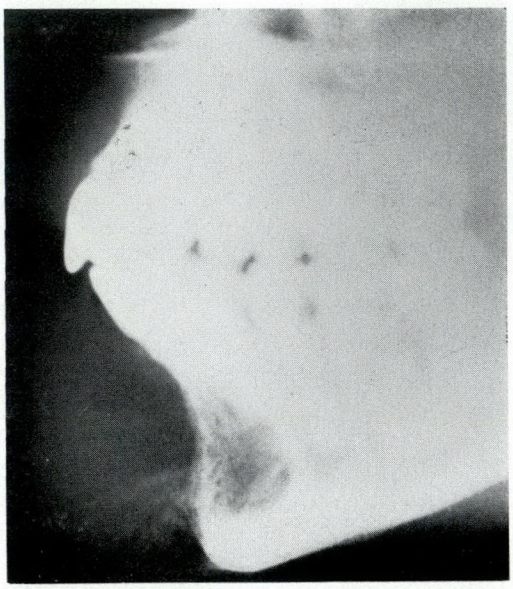

Fig. 1.—Lateral view of the body of the mandible shows a central area of bone destruction and the anteriorly radiating spicules.

radiological diagnosis of osteogenic sarcoma was made. At this time, the lower central incisor teeth had become loose.

This well-developed 15-year-old boy had no detectable abnormalities of his chest, abdomen or extremities. There was no cervical, axillary or inguinal lymphadenopathy. A hard fixed mass, 5 x 7 cm., arose from the symphysis of the mandible and extended laterally on the left to the mental foramen and 1 cm. posterior to the foramen on the right. The mass filled the concavity between the chin and lip (Fig. 2). The overlying skin was fixed to the mass but it was not red or hot. The central two incisor teeth were loose but the mucous membrane was intact even at the site of the previous incision. The gingivolabial sulcus was considerably widened. The chest film was normal. His hemoglobin was 14.3 g./100 ml., leukocyte count was 4300/c.mm.,

*From the Departments of Surgery, Pathology and Diagnostic Radiology, Queen's University, and the Kingston General Hospital, Kingston, Ont.

†Associate Professor of Surgery, Queen's University, Kingston, Ont.

‡Associate Professor of Pathology, Queen's University. Present address: Department of Pathology, University of Western Ontario, London, Ont.

§Associate Professor of Radiology, Queen's University.

Reprint address: Dr. E. E. Sterns, Etherington Hall, Stuart Street, Kingston, Ont.

Fig. 2.—The patient's profile on his first admission showing loss of the normal concavity between the lip and chin.

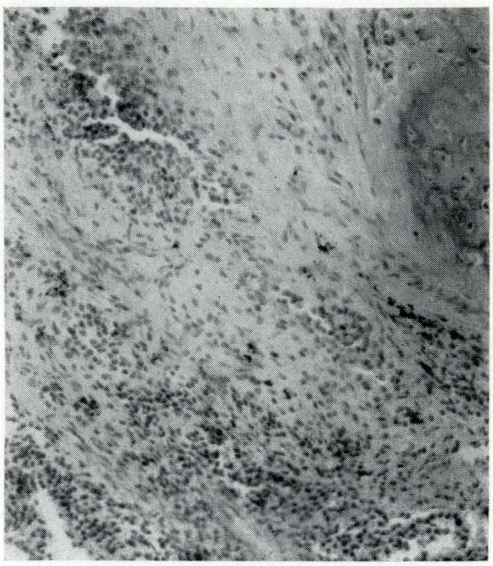

Fig. 4.—The chondromatous tissue (dark-grey islet at the extreme right, upper half of the figure) appears to develop through the stage of hyalinizing connective tissue. Note the immature mesenchymal cells—lower half and upper left (hemalum-phloxine-saffron stains x 126).

erythrocyte sedimentation rate 20 mm. in one hour and alkaline phosphatase 4.7 Bodansky units. The blood smear, differential and urinalysis were normal.

On January 25, 1966 an open biopsy was done under general anesthesia. Microscopically, this invasive tumour was not uniform and consisted of several components, all of which were mesenchymal. The following four distinct components were identified: vascular (Fig. 3), chondromatous (Fig. 4), fibrous (Fig. 5), and mesenchymal cells (Fig. 6). The immature mesenchymal cells gradually "differentiated" into each of the other components. The mesenchymal cells gave rise to the vascular

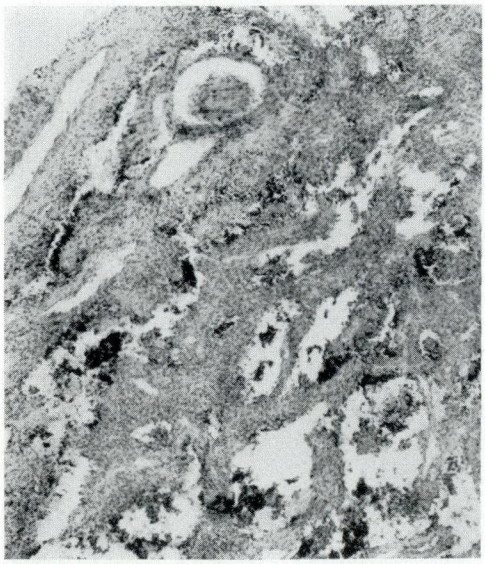

Fig. 3.—In this area the tumour is composed of sheets of mesenchymal cells and vascular channels varying in diameter (hemalum-phloxine-saffron stains x 50).

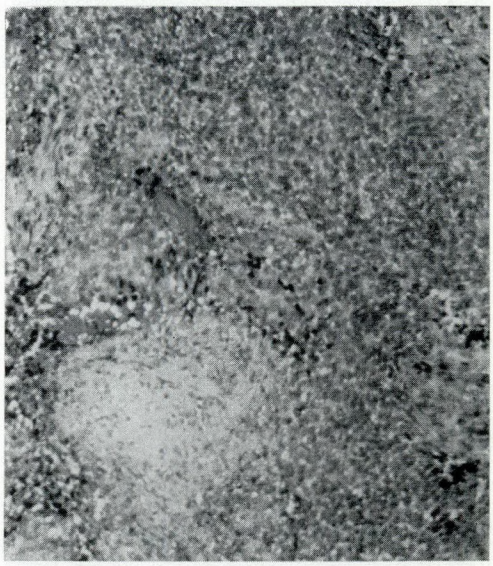

Fig. 5.—An islet of fibrous tissue (pale grey, lower half) situated in an area largely consisting of mesenchymal cells (Masson stain x 125).

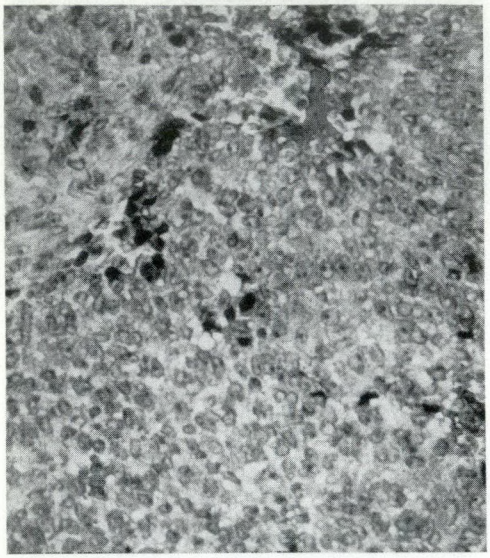

Fig. 6.—This area is dominated by large mesenchymal cells with little stromal support. Some of these cells "differentiate" into the dark, bizarre, endothelial cells that partly line abnormal vascular channels. The contents of one of the channels (upper half, right of centre) stain like serum (Masson stain x 312).

components by one of two ways: they "differentiated" into bizarre endothelial cells which lined tissue spaces creating vascular channels (Figs. 3, 6 and 7). Alternatively, the

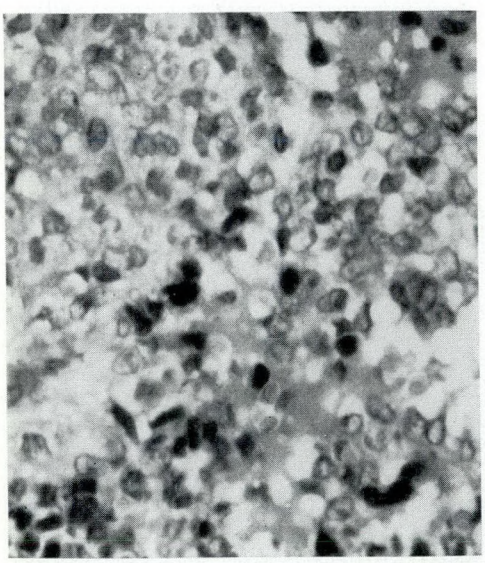

Fig. 7.—Large mesenchymal cells (upper left and middle right) have ill-defined, sparse cytoplasm, vesicular nuclei and prominent nucleoli. They "differentiate" into abnormally configurated, darkly nucleated endothelial cells which in part line the abnormal vascular channels. The latter contain serum-like substance—homogeneous dark grey (hemalum-phloxine-saffron stains x 640).

formation of these vessels mimicked normal angiogenesis; a primitive mesenchymal cell "curled" around its own axis with the nuclear and the scanty cytoplasmic material forming a ring-like structure. The centres of such structures were either empty or contained homogeneous proteinaceous material with the staining quality of serum (Fig. 8). At times, two or three mesenchymal cells participated in the formation of such a ring-like structure. The tumour had a scanty fibrous component,

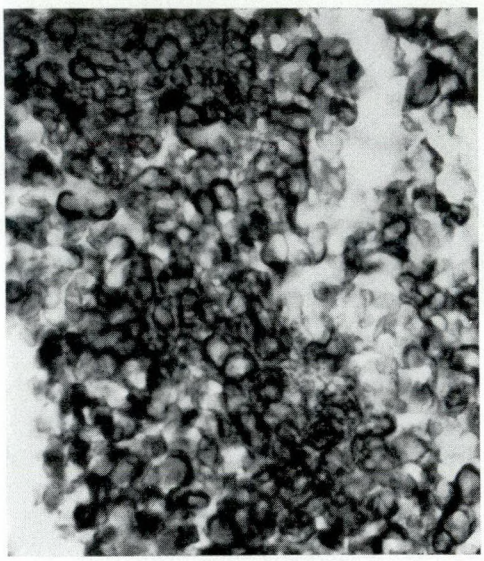

Fig. 8.—Primitive, small vascular channels formed by a process that mimics angiogenesis. Note ring-like structures resulting from curling-up of mesenchymal cells around their own axis leaving a central space. The latter is often not empty but contains homogeneous material similar to serum (Masson stain x 500).

which was in the form of an islet (Fig. 5) or as a precursor of the chondromatous elements (Fig. 4). Both the fibroblasts and the collagen fibres were abnormal. The fibroblasts were large and bizarre, and the collagen bundles varied in thickness, length and degree of hyalinization even within a given area; often an entire islet of fibrous tissue was hyalinized (Fig. 9). The chondromatous component was formed from the mesenchymal cells either through the stage of differentiation to collagenous tissue (Figs. 4 and 10) or directly from the immature mesenchyme. The chondrocytes were bizarre and their maturation did not proceed in orderly fashion (Fig. 11). The elaboration of acid mucopolysaccharides by these cells varied considerably, particularly in areas where the chondromatous tissue arose "directly" from the mesenchymal cells. Calcification of the

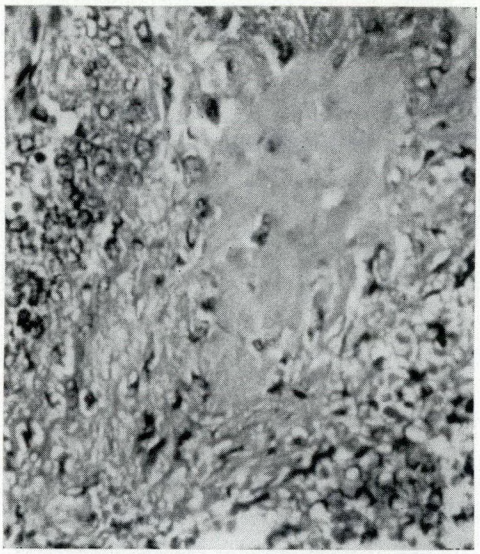

Fig. 9.—An islet of almost completely hyalinized collagenous tissue (hemalum-phloxine-saffron stains x 312).

chondromatous tissue was not prominent. When calcium was found in this tissue (Figs. 4 and 10) it appeared to have been deposited in a haphazard way and there was no orderly process of ossification.

The patient received a course of radiotherapy—^{60}Co teletherapy via three ports: anterior, right and left lateral. Over a five-week period a daily dose of 300 R. was administered to a total of 5354 R. Teeth were extracted in the field of treatment. Within three days, the tumour mass decreased by 25% and by the end of treatment, the mass had completely disappeared. Despite this clinical regression, radiographs of the mandible on February 18 were unchanged, indeed, the bony spicules were more prominent (Fig. 12).

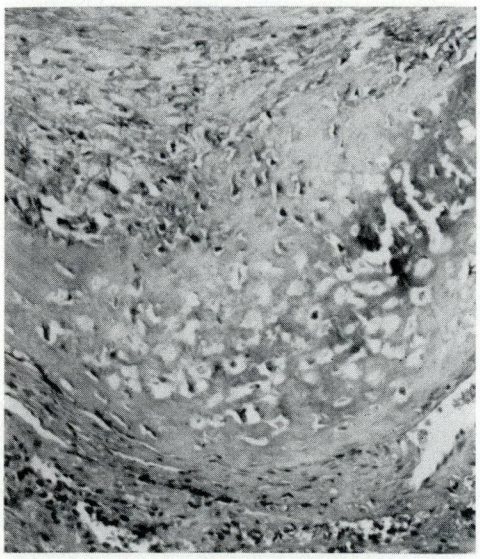

Fig. 10.—Some calcium deposition (extreme right, upper half) in the abnormal chondromatous tissue. There is gradual blending of the latter with the surrounding cellular and fibrous components of the tumour (alcian blue-PAS-orange G-hematoxylin stains x 125).

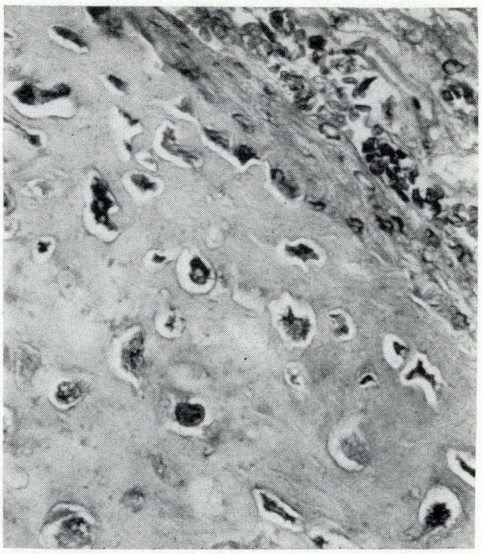

Fig. 11.—Chondromatous component of the tumour shows bizarre cells and a lack of orderly maturation and organization of the tissue (hemalum-phloxine-saffron stains x 720).

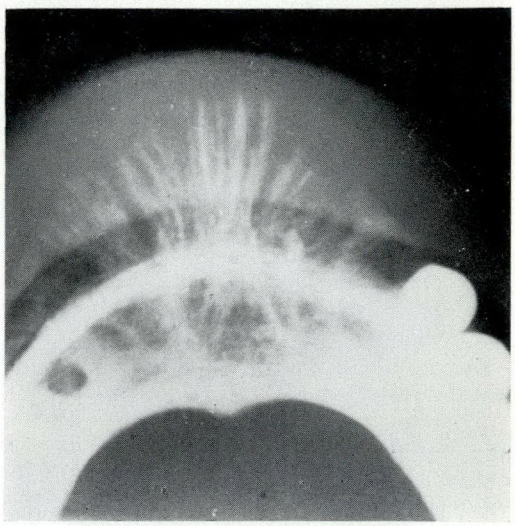

Fig. 12.—Superoinferior view of the body of the mandible. There is a central area of bone destruction. The teeth in the radiation field have been removed. The radiating spicules of bone extend into the soft tissue tumour indicating escape of the neoplasm from the mandible into the adjacent soft tissue.

On March 4, after the radiotherapy had ended, we did another open biopsy under general anesthesia and found no tumour. Despite this reassurance it seemed advisable to resect the mandible.

On March 10 the symphysis and portions of both mandibular rami were resected. The bone was reconstructed using a segment of iliac bone. Tracheostomy and Stamm gastrostomy were also done. The boy suffered no complications during operation or in the immediate postoperative period. Tissue removed during resection showed irradiation changes but no evidence of tumour.

When the interdental wires were removed on April 20, we found a small sinus leading to the central portion of the bone graft.

After discharge, the patient was seen at monthly intervals. His general health remained good and he appeared free of tumour clinically and radiologically. However, it became increasingly evident that the bone graft was infected. The sinus enlarged, his breath was fetid and the graft, originally stable, loosened. He was admitted again on July 30, 1966, not only because of the osteomyelitis but because a left submandibular mass had appeared. On August 3, we excised an enlarged, fibrotic submandibular gland and an adjacent lymph node. Microscopically there was no evidence of tumour. Two days later the bone graft was removed transorally. Within 12 days the sinus closed, his breath was no longer fetid and his chin had begun to recede.

The patient remained well until January 1967, when he developed severe left-sided pleuritic pain, a productive cough, fever, weight loss and increasing dyspnea. Radiographs taken three weeks after the onset of these signs and symptoms showed changes consistent with bilateral pulmonary metastases and a probable left pleural effusion. He had abdominal distension which we thought indicated metastatic involvement of retroperitoneal nodes. He was readmitted to hospital on February 2, 1967.

Despite daily transfusions his hemoglobin stayed below 7 g./100 ml. On February 10, cyclophosphoramide 400 g. daily was started. Two weeks later he was afebrile, his appetite returned, he began to gain weight and his dyspnea became less pronounced. Chest films showed that the mass in the left chest was smaller (it had yielded no fluid on thoracentesis). On February 24 chemotherapy was stopped because of leukopenia. He was well enough to be discharged but he remained well for only two weeks when he was admitted again because of increasing shortness of breath, severe left chest pain and anorexia. A second course of cyclophosphoramide gave no objective or subjective improvement. On June 6, 1967, 18 months after the malignant mesenchymoma was recognized, he died after gradual deterioration. On postmortem examination he had tumour in both lungs and pleural cavities (Fig. 13), which extended retroperitoneally to the left iliac region. Iliac and portal lymph nodes contained tumour. Microscopically, immature mesenchymal cells predominated but the tumour also contained poorly differentiated endothelial channels.

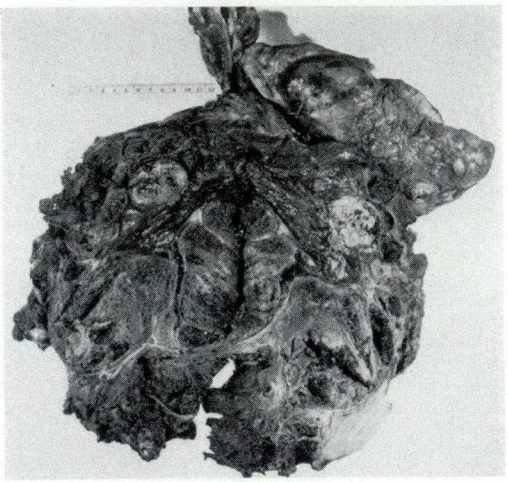

Fig. 13.—Posterior view of the gross specimen of trachea, bronchi and both lungs, removed *en bloc* at necropsy. A sagittal cut made into the left lung shows a large, whitish-grey focus of metastatic tumour. Several smaller tumour nodules are present in the right lower lobe. Note the difference in size between the left (on left) and the right (on right) lung. In addition, the surface of the left lung is shaggy (adhesions, necrosis, hemorrhage), whereas that of the right lung is smooth (reduced approximately 4 x).

Cardiac blood culture grew *E. coli* and large colonies of staphylococci were grown from the lung.

Discussion

Malignant mesenchymoma is a rare neoplasm and, as a primary tumour of bone, is extremely rare. In its clinical manifestations it resembles other malignant bone tumours and has a radiological appearance similar to osteogenic sarcoma. A definitive diagnosis can only be established by histological examination. In the original biopsy, this tumour was composed of angiomatous, primitive mesenchymal, cartilaginous and

fibrous tissue. At post mortem the metastases consisted chiefly of the first two components.

Radiotherapy was selected as the primary treatment and the clinical response was gratifying. When the tissue containing the primary tumour was resected we could demonstrate no residual tumour microscopically. Despite control of the primary tumour, radiotherapy did not prevent dissemination although occult metastases may have been present before radiation. Alternatively, vascular dissemination may have occurred during attempted drainage (before radiation) or at the diagnostic biopsy.

In any event, the primary tumour was radiosensitive. In addition, the patient had an objective remission, albeit temporary, with cyclophosphoramide therapy. After the original treatment he had general improvement in health, reduction in size of the left pulmonary tumour, weight gain, and an increase in hemoglobin values after transfusion. On the other hand, excision of the mandible seemed to make little if any contribution to the management of this particular tumour.

Malignant mesenchymoma affects patients of all ages.[1-6] At the time of discovery the youngest patient was 2 days old,[5] and the oldest 77 years.[1] In a group of 58 patients, only six were older than 20 years. Kauffman and Stout[4] have reported 11 cases considered to be congenital. Seventy-four per cent of malignant mesenchymomas occurred in male patients. Of 38 benign mesenchymomas in children, 26 were in girls and 12 in boys.[7]

Review of the pertinent literature reveals that there is little uniformity in management. Therapy depends on a number of factors, including the size, extent and location of the tumour. There are 50 patients for whom sufficient information on response to treatment is available.[1-7] Of those who survived more than five years and were free of disease, eight had been treated initially by wide excision, one by excision and radiotherapy and one by "enucleation" of the tumour. One patient, treated by primary excision and radiotherapy to metastatic deposits, lived seven years and eight months. Only three patients were treated by radiotherapy alone: all died within 20 months although one child died of poliomyelitis. Twelve patients were treated definitively by incomplete resection with or without radiotherapy. Nine of these died; the longest survival was 28 months. Although three were alive at the time of review, one was moribund 12 months after treatment, one had been followed for only six months and one was well at six years.

The behaviour of the tumour and its response to specific treatment seems to be a function of its histological composition. For this reason, general statements regarding the therapy of malignant mesenchymomas are inappropriate.

References

1. Stout, A. P.: Mesenchymoma, the mixed tumor of mesenchymal derivatives, *Ann. Surg.*, **127:** 278, 1948.
2. Kipkie, G. F. and Haust, M. D.: Malignant mesenchymoma (haemangioblastomyxomatous variety) in a five-year-old boy, *Canad. Med. Ass. J.*, **81:** 179, 1959.
3. Schajowicz, F., Cuevillas, A. R. and Silberman, F. S.: Primary malignant mesenchymoma of bone. A new tumor entity, *Cancer*, **19:** 1423, 1966.
4. Kauffman, S. L. and Stout, A. P.: Congenital mesenchymal tumors, *Cancer*, **18:** 460, 1965.
5. Nash, A. and Stout, A. P.: Malignant mesenchymomas in children, *Cancer*, **14:** 524, 1961.
6. Wilson, F. C. and Parkes, J. C.: Mixed mesodermal tumor (mesenchymoma) of the extremities, *Clin. Orthop.*, **41:** 133, 1965.
7. Le Ber, M. S. and Stout, A. P.: Benign mesenchymomas in children, *Cancer*, **15:** 598, 1962.

Résumé

Il s'agit de l'observation d'un garçon de 15 ans qui présentait un mésenchymome malin du mandibule. Dans la littérature pertinente, ce cas est le troisième d'une tumeur prenant naissance dans l'os et le second mésenchymome malin du mandibule. Cette tumeur était composée de tissue angiomateux, mésenchymateux, chondromateux et fibreux.

La tumeur primaire a bien réagi à la radiothérapie, mais, dans un délai d'une année, sont apparues des métastases pulmonaires qui ont réagi pendant une brève période au cyclophosphamide. L'adolescent est mort 18 mois après le diagnostic. A la nécropsie, on découvrit une tumeur métastatique—ne comprenant que deux des éléments originels, soit du tissu angiomateux et mésenchymateux, dans les poumons, les ganglions lymphatiques, la paroi thoracique et derrière le péritoine.

Les auteurs passent brièvement en revue la littérature des mésenchymomes malins et s'attardent à leur traitement.

GIANT VESICOPROSTATIC CALCULUS: A CASE REPORT*

ARUNAVA CHOUDHURY, M.B., B.S., F.R.C.S.[Eng. & Edin.], *Liverpool, England*

VESICOPROSTATIC calculi are rare. In 1963 Bowers, Calams and Lloyd[1] found six cases and added two of their own. Four more cases were recently reported.[2] The present paper describes one further case—a giant vesicoprostatic calculus.

CASE REPORT

J.C., now 47 years old, had a bladder stone removed at 6 years of age about which no details are available. He had a chronic duodenal ulcer at 26, for which a partial gastrectomy was done at the age of 36. At operation he was found to have gallstones, and a cholecystectomy was also done. The gallstones were pure cholesterol. At 34, he developed cystitis. Subsequent investigation showed that he had bladder-neck obstruction associated with bilateral hydronephrosis and patchy calcification of the prostate. No evidence of systemic disease was found. Tests for tuberculosis and venereal disease were negative. A month later, a prostatic abscess formed and was drained per rectum. Subsequent urethroscopy and urethrography showed a ragged prostatic cavity. His hydronephrosis remained stationary and his blood urea remained normal. A year later he had a suprapubic wedge resection of the bladder neck to ensure free drainage of the bladder. His hydronephrosis improved and his urinary symptoms disappeared, although his urinary infection persisted. Six weeks after operation, he was found to have developed multiple, small calculi in the prostatic cavity, in addition to the previous calcification. These calculi were kept under observation for two years.

In August 1967, 12 years after the wedge resection, he was admitted with a short history of severe "cystitis". He had acute retention and, on rectal examination, a large stony mass was felt in the prostate. A catheter was passed and the bladder emptied very slowly. The urine, which was thick with phosphates, grew *K. aerogenes* and *E. coli*.

A radiograph showed a vesicoprostatic calculus (Fig. 1) but no evidence of back pressure on the kidneys. The blood urea nitrogen was 18 mg./100 ml., serum calcium was 10 mg./100 ml. (on two occasions) and serum phosphate 4.0 mg./100 ml. Ten days after admission, a suprapubic cystolithotomy was done. The bladder was large, adherent and thin-walled. A large stone, seen at the trigone, had a narrow "waist" which extended through the contracted bladder neck to a second portion which lay in a wide prostatic cavity. This hour-glass calculus was 8 cm. long and 5 cm. wide; the narrow waist was only 1 cm. wide. Removal was difficult. After the vesical portion was broken off, the contracted bladder neck was stretched with a hemostat and, with assistance from a finger in the patient's rectum, the prostatic portion was removed. In addition to the prostatic portion of the vesicoprostatic calculus, the prostatic cavity contained a smaller stone. The two had a common faceted surface. The stone was of mixed composition—calcium oxalate and phosphate. The bladder was closed and an indwelling catheter left in place. The patient was treated with ampicillin and acidifying agents.

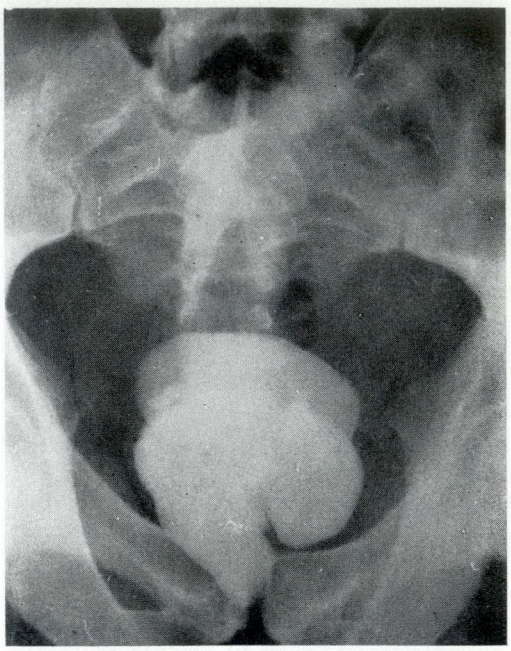

Fig. 1.—A plain radiograph of the pelvis showing the size and the position of the vesicoprostatic calculus.

After two weeks of catheter drainage the suprapubic wound dried up. Although urine leaked from it on two subsequent occasions, the wound dried up promptly with further catheterizations.

*From the Department of Surgery, David Lewis Northern Hospital, Liverpool, England.

Present address: 58/7 Prince Golam Hossain Shah Road, Calcutta 32, India.

Discussion

This man had a long history of urinary tract pathology: a bladder stone in childhood, and bladder-neck obstruction and non-specific, chronic, prostatic infection in adult life. The vesicoprostatic calculus formed after a wedge resection of the bladder neck. Most such stones described in the literature have been in older patients and have developed after open prostatectomy.[1-6] However, they have been encountered in younger patients who had no previous operations;[4, 7, 8] in these, urinary tract infection was blamed.

This patient had stones in the prostatic bed six weeks after wedge resection of the prostate, although symptoms from these stones did not bring him to the doctor for 12 years. Apart from the persistent urinary tract infection, no local or systemic factors were identified which contributed to stone formation. The association of duodenal ulcer naturally drew attention to the parathyroid glands; however, no evidence of hyperparathyroidism was found. Also, the presence of gallstones was fortuitous and did not point to a common systemic factor.

Vesicoprostatic calculus formation requires the following: (1) a dilated prostatic cavity; (2) a narrowed bladder neck; (3) a nucleus for stone formation—loose tags of prostatic tissue or foreign materials, e.g. oxycellulose, portions of catheter or even suture material. "Hanging" bladder stones have been described which form around non-absorbable sutures.[9, 10] Also catgut knots provide the nucleus for such stones. Bladder stones following prostatectomy may have a protein centre,[11] in all probability, remnants of prostatic tissue or catgut; and (4) infection. Abernethy's patient had a previous periurethral abscess[7] and the present case had a prostatic abscess. Infection with a urea-splitting organism alters urine pH and precipitates phosphates; this may lead to stone formation, stagnation and persistence of infection—a vicious circle.

All the above-mentioned factors are present after prostatectomy[2, 12, 13] and after this operation 1% to 3% of patients develop bladder stones.[1] Also, patients who had bladder stones at the time of prostatectomy have a higher incidence of bladder stones subsequently.[11] Twenty per cent of patients who developed bladder stones after prostatectomy, had stones before,[3] and as many as 10 stones had been removed from the bladder at the first operation.[11] In these patients with repeated stones, there was no evidence of hypercalcemia.

The formation of a vesicoprostatic calculus after prostatectomy can be prevented by: (1) wedge resection of a shelf at the bladder neck; (2) use of only fine plain catgut; (3) removal of all dead tissue and foreign materials; (4) eradication of postoperative infection; and (5) acidification of urine to prevent phosphate deposition.

The chain of events in this patient was probably as follows: a stone formed in either the prostatic or bladder cavity around a nidus of suture material or prostatic tissue. Once the nucleus had formed, the stone grew by accretion of urinary mineral salts. The narrow bladder neck subsequently trapped this stone in the prostatic cavity and it grew through into the bladder, producing a characteristic hourglass calculus.

Very large ("giant") vesicoprostatic stones have been described.[3, 7] Labry[4] removed one weighing 80 g. and measuring 8 x 4 cm.

Diagnosis of a vesicoprostatic calculus is made from a history of overflow incontinence, burning sensation over the perineum, passage of stones, phosphates or blood in the urine, a distended bladder and the finding of a hard stony mass in the prostate on rectal examination. Radiographs are confirmatory. The interval between the previous prostatectomy and the recognition of the stone may vary from six months[3] to eight years.[2] Presumably the stone forms soon after the prostatectomy, although the symptoms may be much delayed.

Removal of the stone by transurethral crushing is difficult because the stone cannot be grasped;[1, 7] an attempt to do so may fracture the stone,[8] and traumatize the urethra.

The stone should be removed through a suprapubic operation. Removal of the prostatic portion of the stone is difficult be-

cause of the narrow bladder neck, which must be stretched with a blunt instrument,[2] incised or excised.[8] It is difficult to grasp the stone with an instrument and any attempt to do so may fragment it. Removal by fragmentation has been described,[7] but is not recommended because small fragments may be left behind. It can be extracted digitally with the assistance of pressure from below by a finger in the patient's rectum.

Postoperative complications include recurrent fistula formation, further stone formation and, in the presence of active infection, bacteremia.

Summary

A giant hour-glass calculus occupied the prostatic cavity and part of the bladder—a vesicoprostatic calculus. The patient had had a prostatic abscess and a suprapubic wedge resection of the bladder neck earlier. The pathogenesis of this condition is discussed.

I am grateful to the late Mr. W. R. Hunter, Consultant Surgeon, David Lewis Northern Hospital, Liverpool, England for his kind permission to publish this case and for his encouragement.

References

1. Bowers, L. M., Calams, J. A. and Lloyd, F. A.: Vesicourethral calculus following prostatectomy, *Arch. Surg. (Chicago)*, **86:** 388, 1963.
2. Bridger, J. E.: The 'hour-glass' calculus: vesico-prostatic calculus following prostatectomy, *Brit. J. Urol.*, **39:** 186, 1967.
3. Corbineau: Calcul prostato-vésical, complication éloignée d'une prostatectomie, *J. Urol. Méd. Chir.*, **34:** 199, 1932.
4. Labry, R.: Incontinence d'urine par volumineux calcul vésico-prostatique, *Lyon Chir.*, **40:** 671, 1945.
5. Barbosa de Barros, J.: Cura chirurgica de calculo vesico-prostatico três anos depois de prostatectomia hipogastrica, *S. Paulo Méd.*, **2:** 651, 1932.
6. Caraven and Lourdel: La lithiase vésicale dans les suites de la prostatectomie suspubienne, *J. Urol. Méd. Chir.*, **14:** 111, 1922.
7. Abernethy, D. A.: A large vesical calculus incarcerated in the prostatic urethra, *Brit. J. Urol.*, **16:** 144, 1944.
8. Miller, A.: A case of vesico-urethral calculus, *Brit. J. Urol.*, **17:** 65, 1945.
9. Levack, J. H.: Hanging bladder stones formed on unabsorbable suture and ligature, *Brit. J. Urol.*, **27:** 239, 1955.
10. Weston, B.: Hanging bladder stones, *Brit. J. Urol.*, **29:** 146, 1957.
11. Harrow, B. R.: Vesical calculi following suprapubic prostatectomy, *Amer. Surg.*, **19:** 1184, 1953.
12. Pasquereau: Association français d'urologie XX. Session annuelle tenue à Paris du 6 au 9 octobre, *J. Urol. Méd. Chir.*, **10:** 298, 1920.
13. Lett, H.: On urinary calculus with special reference to stone in the bladder, *Brit. J. Urol.*, **8:** 205, 1936.

Résumé

Un calcul vésico-prostatique siège à la fois dans les cavités vésicale et prostatique. Une fois que la cavité prostatique a été agrandie par prostatectomie ou formation d'un abcès, un calcul peut se former autour d'un nœud de sutures ou du tissu prostatique et, en raison de l'étroitesse du col vésical, prend souvent la forme d'un sablier.

Dans le cas présent, l'homme (47 ans) avait eu une occlusion du col vésical à l'âge de 34 ans. Un abcès prostatique se développa qui fut traité par résection suprapubienne du col vésical. En quelques semaines, de petits calculs se formaient dans la cavité prostatique mais sans donner de symptômes pendant 12 ans.

En août 1967, le malade est hospitalisé pour rétention urinaire aiguë et une grosse masse calculeuse dans la prostate. La radiographie montre la présence d'un gros calcul vésico-prostatique.

A l'exploration suprapubienne, on constate que le calcul affecte la forme d'un sablier. La partie vésicale est détachée et la partie prostatique enlevée par étirement du col vésical, à l'aide d'une pression digitale par le rectum. Opéré, le malade eut besoin d'un drainage vésical continu pour permettre à la fistule urinaire suprapubienne de se cicatriser.

TRAUMATIC RUPTURE OF THE RIGHT DIAPHRAGM: REPORT OF A CASE*

J. K. Y. YAO, M.D., F.R.C.S.[C]† and L. J. MAHONEY, M.D., F.R.C.S.[C],‡
Toronto, Ont.

WITH an increasing number of vehicular and industrial accidents and with improved resuscitation for the seriously injured, rupture of the diaphragm is being seen more frequently. This condition should be kept constantly in mind.

In 98% of the reported cases the left hemidiaphragm was involved.[1] Even in the few patients with right-sided rupture, the presence of the liver on that side usually prevented extensive herniation of abdominal contents into the thorax.

At St. Michael's Hospital, Toronto, we recently treated a man with right-sided diaphragmatic rupture and herniation of numerous abdominal organs in whom the onset of symptoms was delayed. This delay made diagnosis difficult and complicated the surgical approach. Theoretically it would be easier to repair the diaphragmatic defect through a thoracotomy, but the adhesions in the abdomen in long-standing herniation would be difficult to release.

CASE REPORT

R.S., a 21-year-old man, had been involved in a car accident four years before. At that time, he fractured two ribs on the left side and also fractured his pelvis. With conservative treatment he recovered and was well until four or five months before the present admission, when he began to have episodes of "indigestion" and "gaseous distension". An upper gastrointestinal series done at that time was interpreted as demonstrating "pyloric obstruction". He was treated with antacids with some relief. Two weeks before admission, he had several brief attacks of mild epigastric

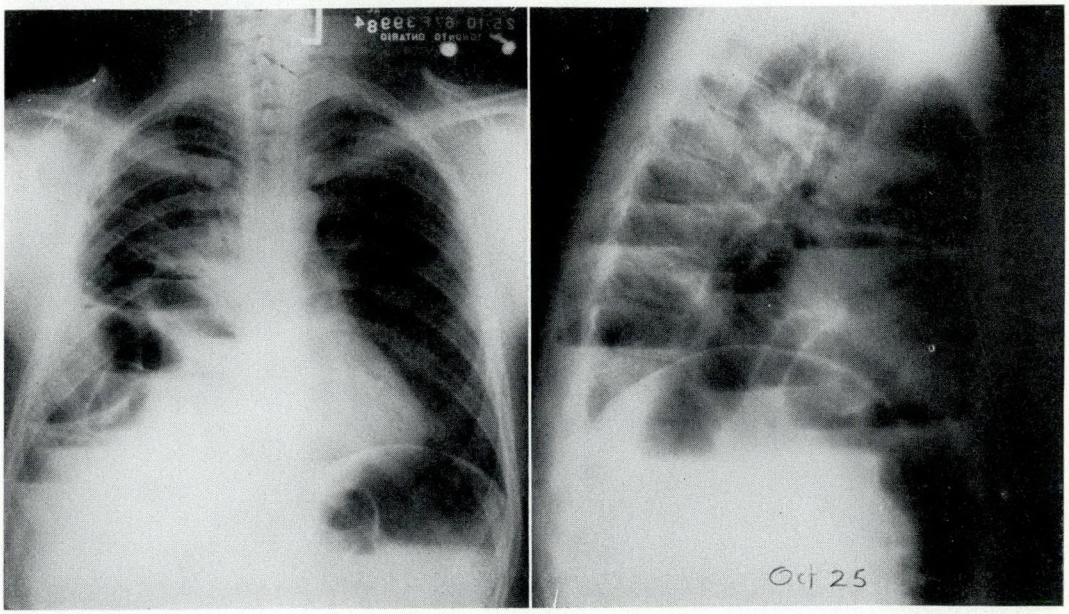

Fig. 1a **Fig. 1b**

Fig. 1.—(a) Posteroanterior and (b) lateral roentgenograms of the chest showing the characteristic picture of a diaphragmatic rupture: (a) an arch-like shadow resembling an abnormally high diaphragm; (b) air-fluid levels above the usual level of the diaphragm; and (c) shift of the heart and mediastinum to the left. Note also the large volume of air and fluid in the stomach.

*From the Department of Surgery, University of Toronto, and St. Michael's Hospital, Toronto, Ont.
†Clinical Teacher, Division of Cardiovascular and Thoracic Surgery, University of Toronto.
‡Assistant Professor, Department of Surgery, University of Toronto.

pain which subsided spontaneously. Three days before admission he began to vomit repeatedly, bringing up sour yellowish material. This was associated with severe crampy periumbilical pain and dyspnea. He obtained relief by sitting up and leaning forward.

On admission to Penetanguishene General Hospital, Penetanguishene, Ontario, he was acutely distressed and had moderate dyspnea. He was afebrile. Breath sounds were absent from the right chest, but bowel sounds were present in the lower one-half. The apex beat was at the left anterior axillary line. The abdomen was moderately distended and mildly tender. Bowel sounds could not be heard in the abdomen. The only pertinent laboratory finding was an elevated leukocyte count (19,200/c.mm.).

The attending physician made a tentative diagnosis of "partial bowel obstruction secondary to a diaphragmatic rupture". Plain films of the chest confirmed the presence of bowel in the chest (Fig. 1). The patient was then transferred to St. Michael's Hospital, Toronto.

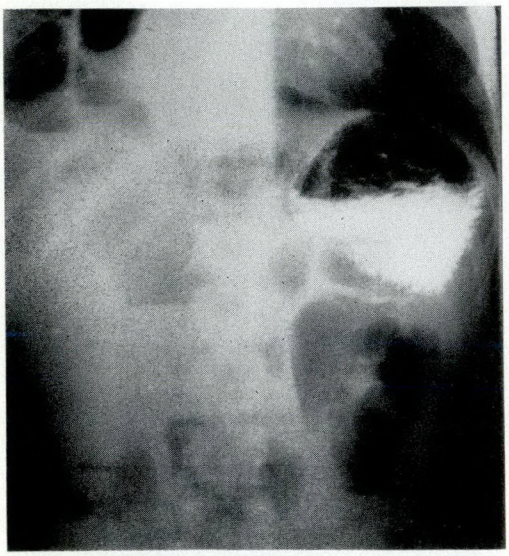

Fig. 2.—Upper gastrointestinal series showing that no barium has passed out of the gastric fundus over a 90-minute period, even with the patient standing.

While in the Emergency Department, a Levin tube was passed and 2500 c.c. of green-yellow fluid was removed, giving immediate symptomatic relief. The elevated leukocyte count returned to normal the following day, perhaps in response to intravenous fluids given on admission. Upper gastrointestinal radiographs were made. Over a 90-minute period, no barium passed out of the fundus of the stomach (Fig. 2). When the patient was put

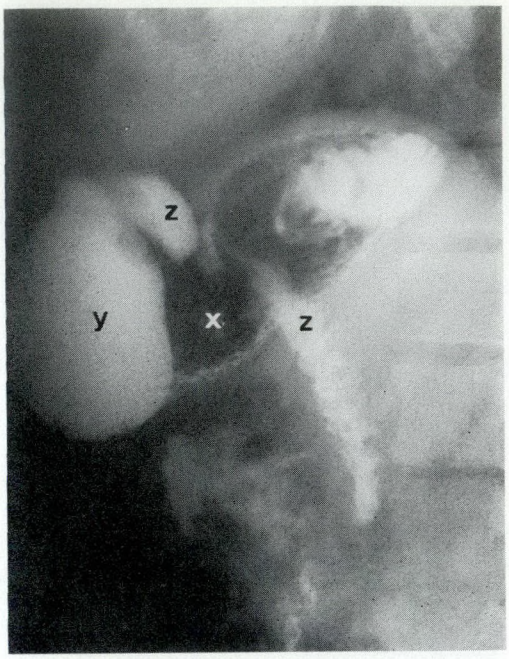

Fig. 3.—When the patient was placed in the right lateral position and his head elevated, barium flowed into the body (x) and antrum (y) of the stomach, and the duodenum (z). Organoaxial volvulus of the stomach is well demonstrated.

in the right lateral position with his head elevated, the barium flowed into the body and antrum of the stomach and subsequently, passed without hindrance into the duodenum. In the films the pylorus was seen to lie in close proximity to the cardia (Fig. 3). Because

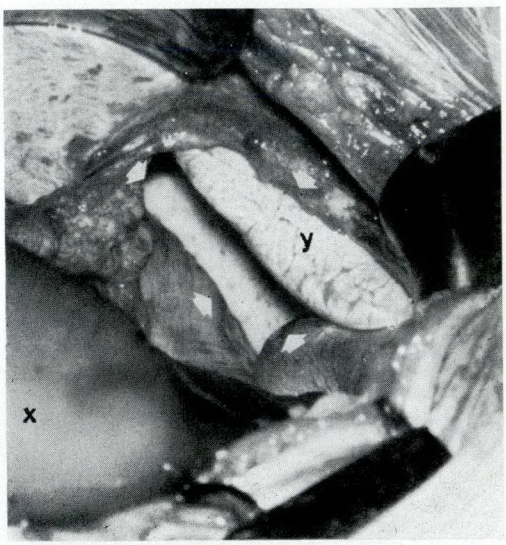

Fig. 4.—At operation, the liver is retracted downwards by the hand (x) to show the defect in the diaphragm (arrows) and part of the lung protruding through the defect (y).

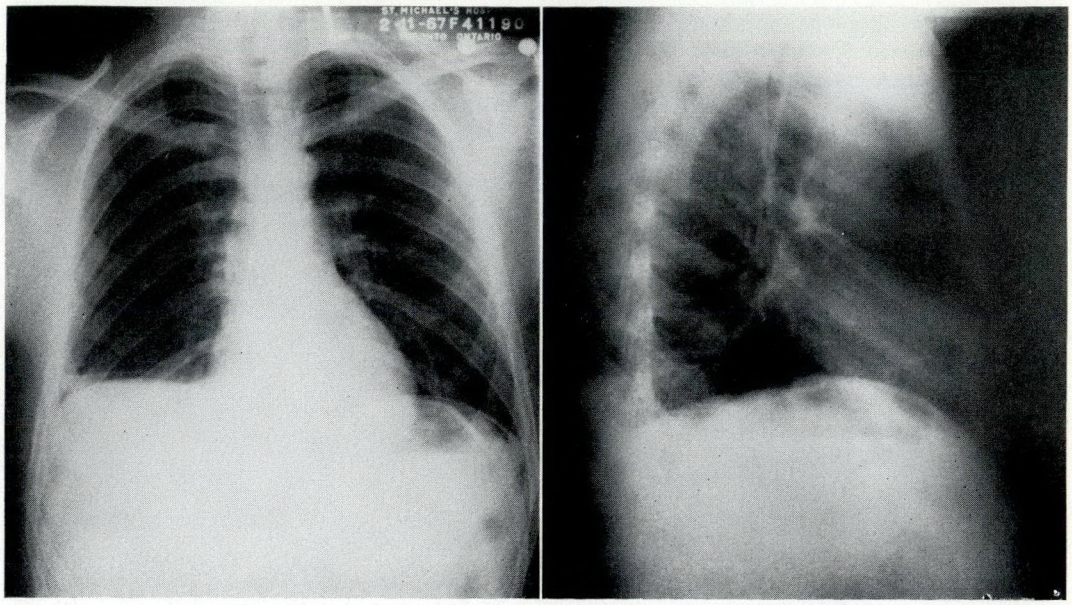

Fig. 5a Fig. 5b

Fig. 5.—(a) Posteroanterior and (b) lateral roentgenograms of the chest after operation.

of the volvulus of the stomach and because of the possibility of extensive adhesions, we decided to approach this lesion through an upper right paramedian abdominal incision and prepare for a separate thoracotomy if necessary.

On exploration, we found that the stomach was folded upon itself along the transverse axis and held there by dense adhesions, which were released with some difficulty. Besides the stomach, the transverse colon, the left lobe of the liver, part of the right lobe of the liver, the gallbladder, loops of small intestine and omentum were in the right thoracic cavity. The defect in the diaphragm, approximately 15 cm. in diameter, was in the region of the central tendon (Fig. 4). Parts of the abdominal organs were adherent to the edges of the defect. Fortunately, there were only a few filmy adhesions between these and the lung, which was re-expanded without difficulty (Fig. 5). The defect was overlapped and closed with interrupted heavy silk sutures. The patient's postoperative course was uneventful.

Discussion

Ambrose Paré in 1579 first described traumatic rupture of the diaphragm. Since then, this injury has been reported frequently in the literature.[1-4] However, right-sided lesions are rare[1] and each may present a different variation in the clinical or pathological picture.

In 1959, Grage, MacLean and Campbell[5] were able to collect only 12 cases of right-sided rupture in the English literature. Schwindt and Gale[6] described 12 patients with traumatic rupture, but only one involved the right side. Noon, Beall and De Bakey[7] reported 22 cases in 1966; of these, only four were on the right side. Waldhausen *et al.*[8] in a series of 23 cases found only three on the right side. Bernatz, Burnside and Clagett[9] reported 112 patients with diaphragmatic rupture; only eight were on the right side. Most right-sided diaphragmatic ruptures do not contain abdominal viscera because of the presence of the right lobe of the liver.

In general, patients with diaphragmatic rupture whose symptoms are delayed have vague, chronic abdominal complaints. However, occasionally, sudden obstruction or strangulation of a viscus may develop.

Radiologically, the diagnosis is suspected if the chest films reveal the following pattern, described in 1951 by Carter, Giuseffi and Felson:[10] (1) an arch-like shadow resembling an abnormally high diaphragm; (2) extraneous shadows such as gas bubbles or other abnormal markings above the usual level of the diaphragm; (3) shift of the heart and mediastinal structure to the side opposite that of the defect and (4)

disc- or plate-like areas of atelectasis in the lung adjacent to the arch-like shadow. To these, Arbulu, Read and Berkas[3] have added presence of fluid levels in the affected hemithorax. Barium studies will confirm the presence of bowel in the chest.

Surgical repair is usually indicated. Because it may be necessary to decorticate the lung to obtain complete re-expansion, and because of its technical ease, the thoracic approach is usually recommended. However, in this patient, because of the gastric volvulus and possible dense adhesions, we preferred the abdominal approach. In long-standing rupture, the diaphragm may be atrophic and, in these patients, prosthetic patches may be necessary to close the defects.[8]

Summary

A young man had a closed traumatic rupture of the right leaf of the diaphragm with herniation of numerous abdominal organs. The onset of his symptoms was delayed. This rare condition, if unrecognized, may cause serious complications.

We gratefully acknowledge the help of Dr. Peter Brasher of Penetanguishene General Hospital, Penetanguishene, Ontario, who made the initial diagnosis and referred this patient to us. Dr. N. Patt of the Department of Radiology kindly reviewed the radiographs with us.

References

1. Ebert, P. A., Gaertner, R. A. and Zuidema, G. D.: Traumatic diaphragmatic hernia, *Surg. Gynec. Obstet.*, **125:** 59, 1967.
2. Alivisatos, C. N. *et al.*: Traumatic closed rupture of the diaphragm, *Dis. Chest*, **46:** 435, 1964.
3. Arbulu, A., Read, R. C. and Berkas, E. M.: Delayed symptomatology in traumatic diaphragmatic hernia with a note on eventration, *Dis. Chest*, **47:** 527, 1965.
4. Sterns, L. P., Schmidt, W. R. and Jensen, N. K.: Traumatic rupture of the right leaf of the diaphragm, *Dis. Chest*, **51:** 205, 1967.
5. Grage, T. B., MacLean, L. D. and Campbell, G. S.: Traumatic rupture of the diaphragm; a report of 26 cases, *Surgery*, **46:** 669, 1959.
6. Schwindt, W. D. and Gale, J. W.: Late recognition and treatment of traumatic diaphragmatic hernias, *Arch. Surg. (Chicago)*, **94:** 330, 1967.
7. Noon, G. P., Beall, A. C. and De Bakey, M. E.: Surgical management of traumatic rupture of the diaphragm, *J. Trauma*, **6:** 344, 1966.
8. Waldhausen, J. A. *et al.*: The diagnosis and management of traumatic injuries of the diaphragm including the use of Marlex prostheses, *J. Trauma*, **6:** 332, 1966.
9. Bernatz, P. E., Burnside, A. F. and Clagett, O. T.: Problem of the ruptured diaphragm, *J. A. M. A.*, **168:** 877, 1958.
10. Carter, B. N., Giuseffi, J. and Felson, B.: Traumatic diaphragmatic hernia, *Amer. J. Roentgen.*, **65:** 56, 1951.

Résumé

Un jeune homme qui avait été victime d'un accident d'auto quatre ans plus tôt, a été hospitalisé pour un volvulus de l'estomac et une occlusion partielle. Après examen plus poussé, on découvre une rupture du diaphragme portant sur le côté droit. Au moment de l'opération, on note que l'estomac, le lobe gauche du foie, la vésicule biliaire, le côlon transverse, des anses du grêle et l'épiploon sont tous situés dans la partie droite de la cavité thoracique. On répare le défaut par une incision abdominale. Les auteurs passent brièvement en revue la littérature relative à cette pathologie.

ECTOPIC SPLENIC TISSUE IN THE GONAD: A CASE REPORT*

M. QUINN HILL, M.B., Ch.B., C.R.C.P.[C], *Willowdale, Ont.*

Ectopic splenic tissue in the gonad is a rare congenital malformation seen most commonly in the male. It has clinical significance because it enters the differential diagnosis of tumours of the left testicle.

Case Report

On a routine physical examination by his family doctor, this otherwise healthy 13-year-old white boy was found to have a firm swelling within the upper pole of the left testicle. A provisional diagnosis of testicular tumour was made and the boy referred to a urological surgeon. The left side of the scrotum was subsequently explored.

A definite, firm swelling occupied the upper one-third of the testicle and seemed to be completely within the tunica albuginea and a vestigial epididymis lying laterally.

Fig. 1.—The nodule with prominent malpighian corpuscles occupies the upper one-third of the testis and impinges on the rete testis. The surgeon's diagnostic incision is present within the splenic nodule (H & E).

Fig. 2.—Seminiferous tubules abut the intact capsule of the splenic nodule (H & E x 100).

The testicle and epididymis weighed 28.5 g. and measured 4.0 x 3.5 x 2.5 cm. A hemorrhagic, red-brown nodule 1.8 cm. in diameter, covered by the tunica albuginea, deformed the upper pole and impinged on the rete testis. On section, the nodule resembled choriocarcinoma. The seminiferous tubules were yellow, but did not "string". The epididymis was formed by small ductules embedded in yellow, loose fat applied to the posterior part of the testicle.

On microscopic examination the red-brown nodule was formed by mature, encapsulated splenic tissue (Fig. 1). Collagenous trabeculae, malpighian corpuscles complete with penicillar arteries and venous sinuses in the red pulp were readily identified. The collagenous capsule of the splenic tissue displaced the seminiferous tubules and part of the rete testis (Fig. 2). Spermatogonia showing mitotic figures lined the seminiferous tubules. Mature sperma-

*From the Department of Pathology, North York General Hospital, Willowdale, Ont.

tozoa, however, were not seen either in the seminiferous tubules, the epididymis or the rete testis. The epididymal tubules, though few in number, were histologically normal.

Discussion

Bostroem[1] in 1883 first described this condition. In 1956 Putschar and Manion[2] collected 30 cases from the literature and subdivided the anomaly into two groups: the "continuous", in which there is an anatomical continuity with the main spleen; and the "discontinuous", in which there is isolated splenic tissue in the inguinal canal or gonad. The present case belongs in the discontinuous group.

To date this condition has been described only on the left side. There is a large male predominance, perhaps because the testicle is so accessible; however, this condition has been described in the female.[3]

By 1968 the number of reported cases had risen to 52. Watson[4] collected all published cases and analyzed the other abnormalities known to coexist with this anomaly. Local defects were common particularly with the continuous type—indirect hernia recognized at operation in 16 of 38 cases, and various degrees of ectopia of the testicle. A significant number (11 out of 52) had severe bone defects, notably micrognathia and bony defects of the limbs. All these defects are more common with the continuous type. This association is usually ascribed to the coexistent occurrence during gestation of: the descent of the gonad; the rotation of the left dorsal mesogastrium containing the splenic precursor; and the appearance of Meckel's cartilage and the limb anlages. It is postulated that a teratogenic stimulus acting at this time (the 20-mm. embryo) produces these associated congenital defects. In none of the males described to date was traumatic dissemination of splenic tissue thought to be an etiologic factor, although the solitary woman had had an abdominal operation. The possibility that the splenic tissue in the ovary had been implanted during operation may cast doubt on the existence of this entity in women.

Summary

A 13-year-old boy is described who had ectopic splenic tissue in the left gonad. Apart from the association with other congenital defects, this anomaly has a clinical significance in the differential diagnosis of tumours of the left testicle.

I wish to acknowledge the aid of Drs. R. C. Ritchie (Chief Pathologist) and S. Gordon of North York Branson Hospital.

References

1. Bostroem, E.: Gesellschaft Deutscher Naturforscher und Arzte. Verhandlungen der 56. Versammlung, Freiburg, 1883, p. 149.
2. Putschar, W. G. J. and Manion, W. C.: Splenic-gonadal fusion, *Amer. J. Path.*, **32:** 15, 1956.
3. Almenoff, I. A.: Splenic-gonadal fusion, *New York J. Med.*, **66:** 1679, 1966.
4. Watson, R. J.: Splenogonadal fusion, *Surgery*, **63:** 853, 1968.

Résumé

La présence de tissu splénique ectopique dans les gonades mâles est une anomalie congénitale fort rare. Dans le cas présent, chez un adolescent de sexe masculin, l'auteur, au cours d'un examen clinique banal, a découvert une masse dans un testicule. Le testicule a été enlevé. A l'examen histologique, cette masse était constituée de tissu splénique ectopique. L'auteur passe brièvement en revue la littérature sur le sujet.

EXPERIMENTAL SURGERY

MECHANICAL AUGMENTATION OF CORONARY CIRCULATION IN THE ISCHEMIC HEART*

SHEKHAR CHATTERJEE, M.D., M.S., M.Sc. and
JACOB ROSENSWEIG, M.D., C.M., F.R.C.S.[C], F.A.C.S., *Montreal, Que.*

COUNTERPULSATION[1] is a mechanical method for assisting circulation and augmenting aortic diastolic pressure. Blood is phasically withdrawn from the aorta during systole and reinfused during diastole. Since coronary flow is primarily a diastolic phenomenon, elevation of diastolic pressure increases coronary flow and collateral circulation to ischemic myocardium.[2, 3] The following experiments were carried out to study mechanically induced coronary collateral circulation and to determine its hemodynamic and functional significance.

MATERIALS AND METHOD

Chronic coronary insufficiency was produced by applying ameroid constrictors (2.77 mm. internal diameter) about the origin of the anterior descending and circumflex branches of the left coronary artery. Because 50% or more of the lumen is constricted within two weeks, we applied counterpulsation arbitrarily on the fourteenth day for one hour using the SIMAS unit,† a computer-programmed, hydraulically actuated pump.

Experiment 1–Survival Study

Of the 19 adult, mongrel dogs operated upon, nine served as controls. Through a left thoracotomy, ameroid constrictors were placed about the origin of the anterior descending and circumflex branches of the left coronary artery. Treated dogs were counterpulsated on the fourteenth day (Fig. 1). The dogs were followed until death, but "long-term" survivors were killed after 90 days. At autopsy, we made coronary angiograms and took myocardial sections for histological examination.

Experiment 2–Hemodynamic Study

Ten adult, mongrel dogs were operated upon–five served as controls. As in Experiment 1, ameroid constrictors were placed on the coronary arteries. In addition, an electromagnetic flow probe was applied about each coronary artery, 3 to 4 cm. distal to the constrictor (Fig. 1a). Treated dogs were counterpulsated on the fourteenth day. Flow was recorded at intervals throughout the study period and the surviving dogs were killed after 30 days. At autopsy the same examinations were carried out as in Experiment 1.

Experiment 3–Metabolic Study

Five adult, mongrel dogs were operated upon. The ameroid constrictors were applied and blood samples were drawn from the aorta and the coronary sinus for lactate and pyruvate determinations.

On the fourteenth day, through a right thoracotomy, we inserted a cannula into the coronary sinus and exteriorized its distal end (Fig. 1b). After the chest wall was closed, counterpulsation was carried out for one hour. Aortic and coronary-sinus blood samples were drawn for lactate and pyruvate determinations immediately before and after counterpulsation. These determinations were subsequently repeated on coronary sinus blood daily for three days.

RESULTS

Experiment 1–Survival Study

Seven of the nine control animals died within 30 days of placement of coronary artery constrictors; the other two died on the thirty-second and forty-fifth day respectively. In contrast, all treated dogs sur-

*From the Departments of Surgery, Lady Davis Institute for Medical Research, Jewish General Hospital, and Experimental Surgery, McGill University, Montreal, Que.

Supported in part by grants from the Quebec Heart Foundation and the Medical Research Council of Canada.

†Hamilton Standard Division of United Aircraft, Farmington, Conn.

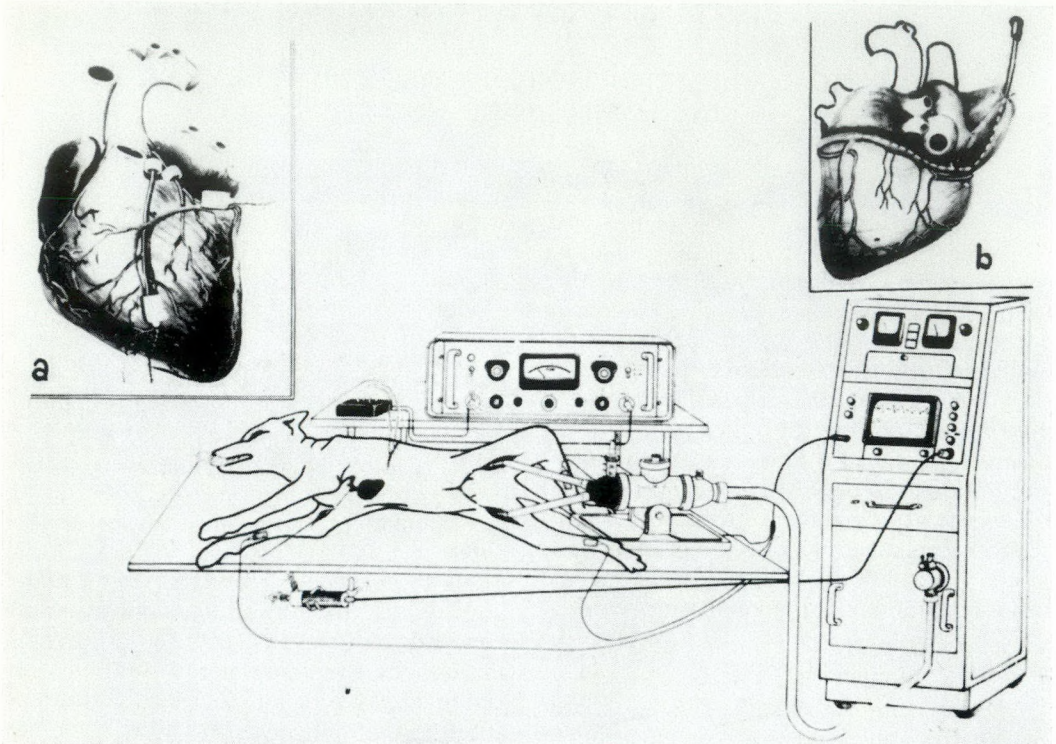

Fig. 1.—Schema for counterpulsation. Insert (a) shows the position of the ameroid constrictor and flow probe on the anterior descending and left circumflex artery in Experiment 2 and (b) shows the technique of implanting the coronary sinus catheter in Experiment 3.

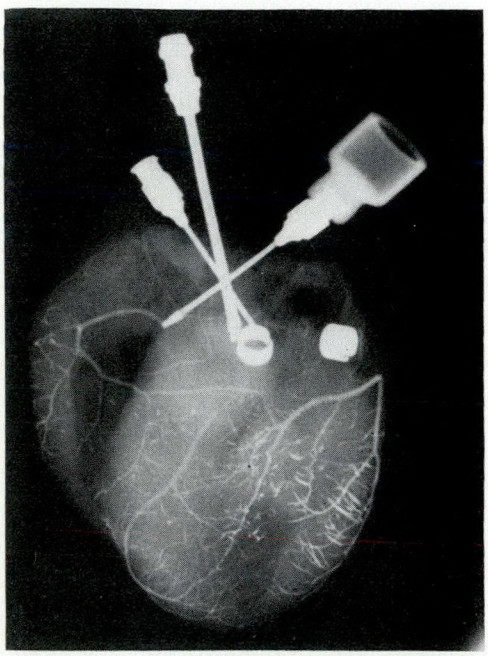

Fig. 2a

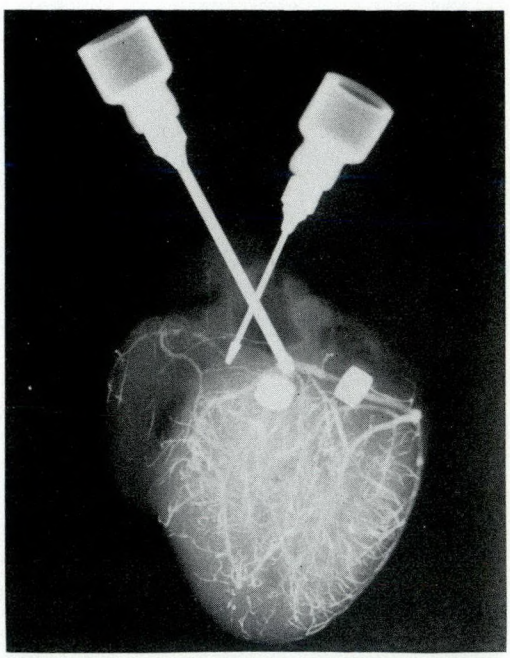

Fig. 2b

Fig. 2.—Angiograms of counterpulsated dogs showing the three primary sources for collateral circulation to the anterior descending and left circumflex arteries: (a) retrograde filling from the right coronary artery; (b) perfusion from the septal artery; and diagonal, anterior, left ventricular branches arising proximal to the constrictors.

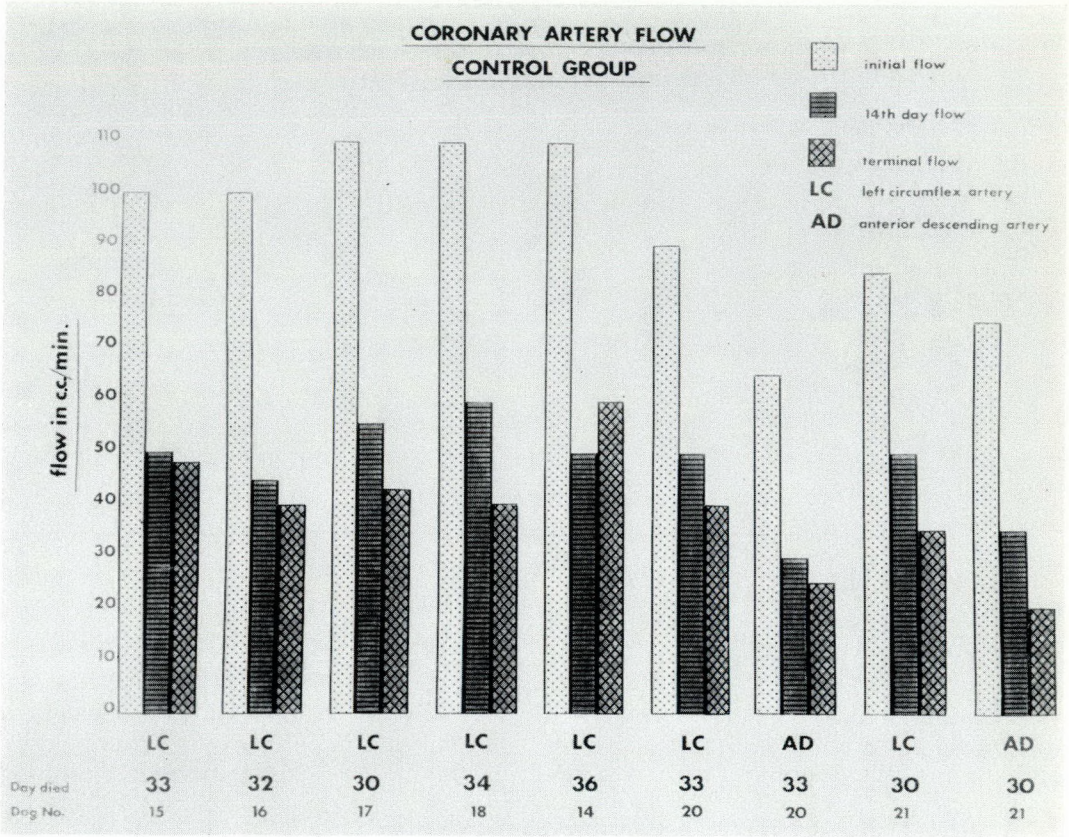

Fig. 3.—Control animals: initial coronary flow, 14-day flow, and final flow before death.

vived 30 days and 80% lived more than 37 days. Despite complete, proximal, coronary artery occlusion, 60% lived until they were sacrificed after three months.

Angiographic studies in control animals showed no evidence of prominent collateral circulation, but in treated dogs increased flow was apparent. We detected three primary sources for collateral circulation: the right coronary artery, the septal artery and the diagonal, anterior, left ventricular branches, which arise directly from the left main coronary artery proximal to the constrictors (Fig. 2).

Experiment 2—Hemodynamic Study

After the ameroid constrictors were applied, coronary flow fell in both groups, decreasing to an average of 49% by the fourteenth day. In control dogs the flow diminished only slightly thereafter despite increasing proximal stenosis. At the final determination before death, coronary flow averaged 41% (Fig. 3).

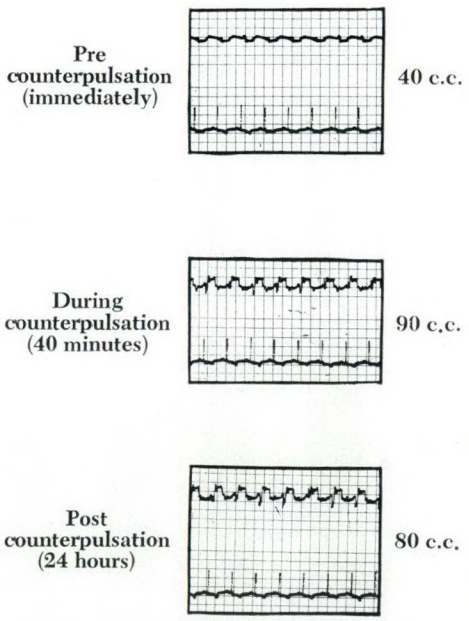

Fig. 4.—Flow tracing demonstrating increased flow after 40 minutes of counterpulsation. Amplitude of flow during diastole is increased, and the polarity is reversed.

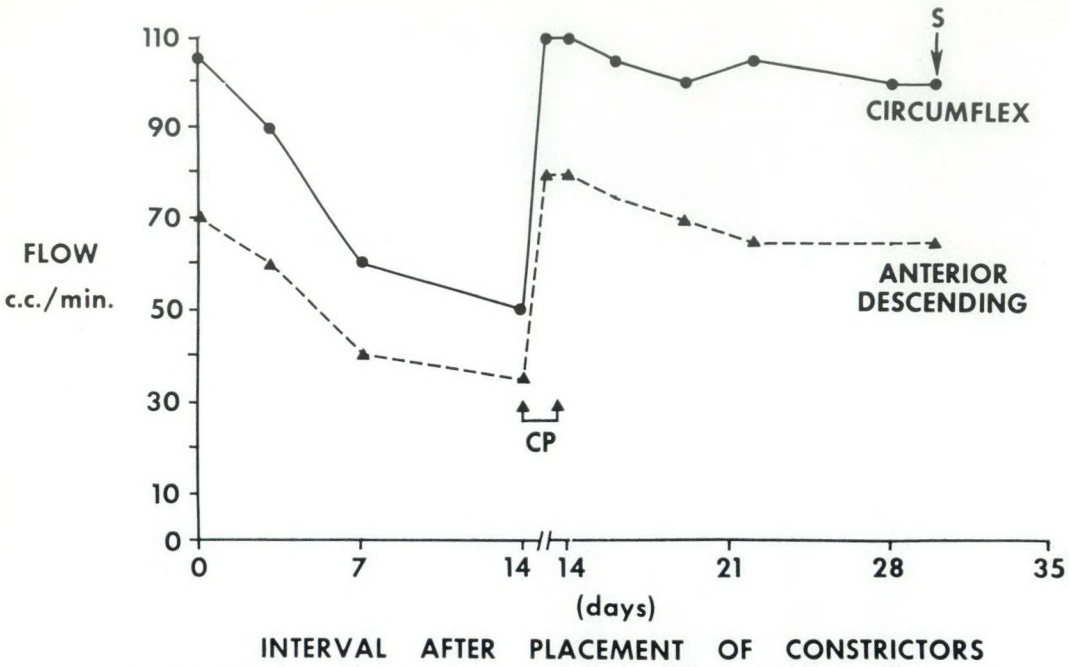

Fig. 5.—Typical coronary flow curves in dogs treated by counterpulsation.

In the treated group, counterpulsation dramatically restored the flow towards normal and the increased flow was apparent within 30 minutes. Coincident with the increase in coronary flow, the polarity in the flow tracings reversed, indicating

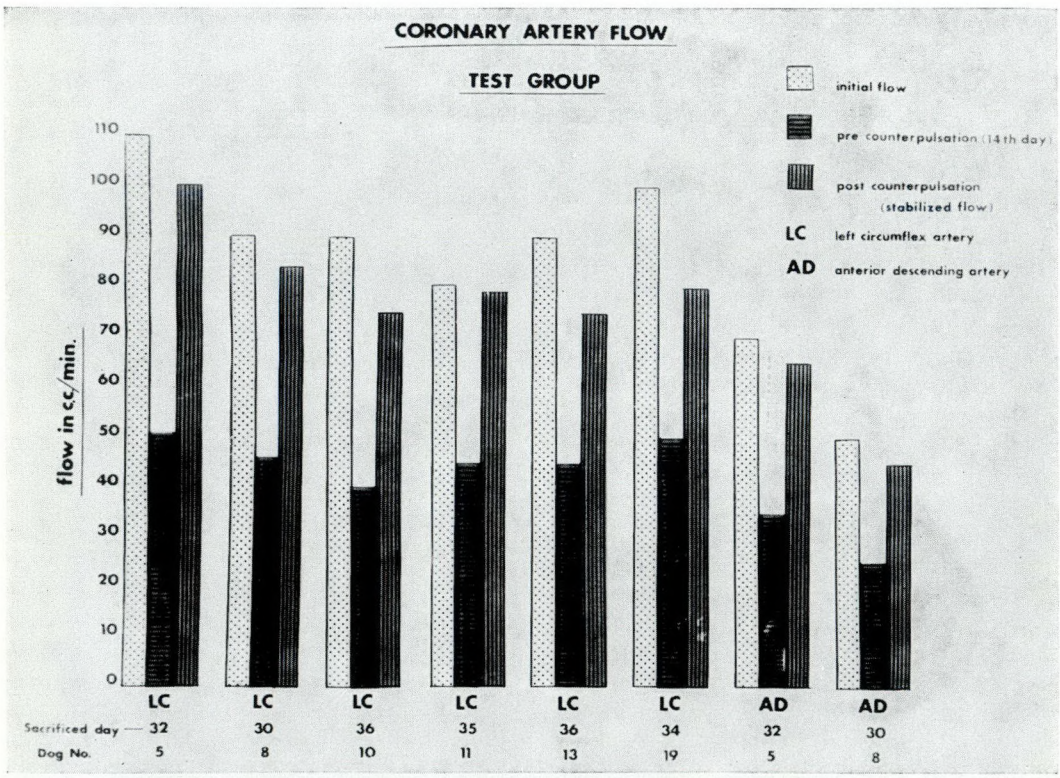

Fig. 6.—Treated dogs: initial, pre-counterpulsation and post-counterpulsation coronary flow.

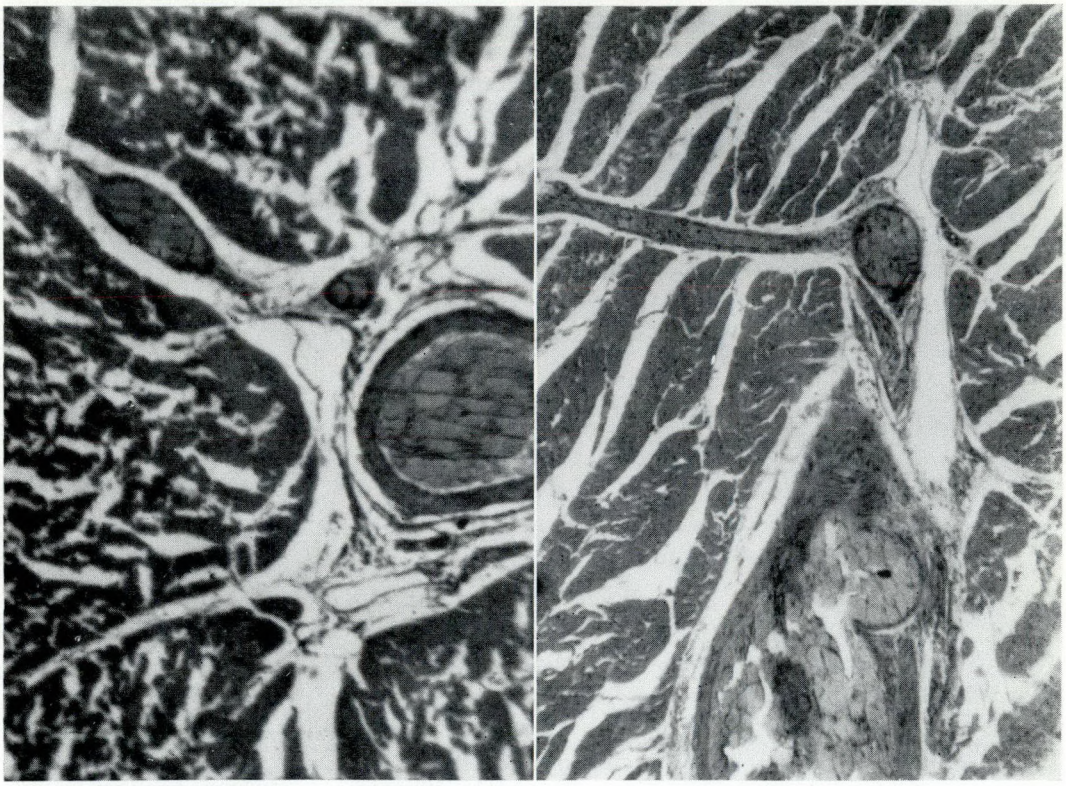

Fig. 7a Fig. 7b

Fig. 7.—Photomicrograph showing the calibre of (a) septal and (b) left ventricular intramyocardial arteries and arterioles in a treated dog.

that the direction of flow had reversed in the distal portion of the occluded arteries (Fig. 4). The coronary flow subsequently diminished gradually over several days and then stabilized at a mean of 89% of the initial flow (Figs. 5 and 6). Angiograms subsequently showed that retrograde filling of the occluded arteries came from the same three sources mentioned previously; namely, the right coronary artery, the septal artery, and diagonal, anterior, left ventricular branches arising proximal to the constrictors. On histological examination, we found myocardial infarction in four control dogs, but in none of the counterpulsated animals. The hearts of treated dogs showed increased prominence and numbers of subepicardial and intramyocardial arteries and arterioles (Fig. 7).

Experiment 3—Metabolic Study

Lactate concentration in the arterial and coronary sinus blood rose progressively after we applied coronary artery constrictors and produced increasing myocardial ischemia. Initially, mean lactate concentration was greater in arterial blood (arterial 2.64 mM./l., coronary sinus 2.23 mM./l.) and excess lactate was −0.32 mM./l. However, by the fourteenth day, just before counterpulsation, the mean lactate concentration was greater in the coronary sinus blood (arterial 3.48 mM./l., coronary sinus 3.68 mM./l.) and there was excess lactate (+0.20 mM./l.). Obviously the myocardium had stopped extracting lactate and was now producing it. After counterpulsation the lactate concentration declined (arterial 2.42 mM./l., coronary sinus 2.17 mM./l.) and the excess disappeared (−0.12 mM./l.), indicating that normal oxidative metabolism had been re-established (Figs. 8 and 9).

Discussion

The results of these experiments demon-

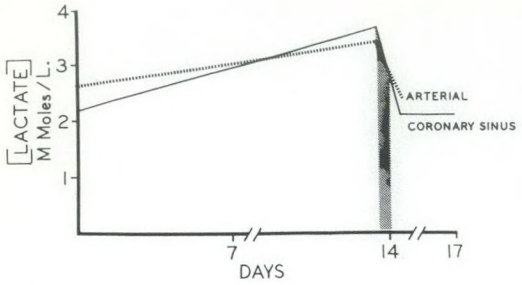

Fig. 8.—Effect of counterpulsation on arterial and coronary-sinus lactate concentration in the ischemic heart.

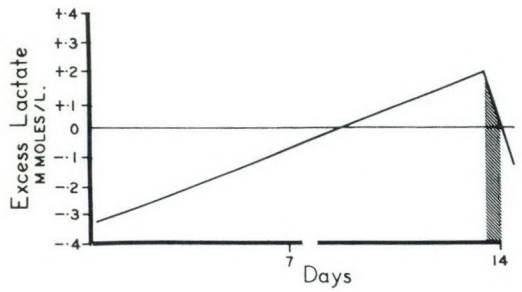

Fig. 9.—Effect of counterpulsation on excess lactate concentration in the ischemic heart.

strate that, despite critical, proximal, coronary artery stenosis, counterpulsation can restore blood flow to the ischemic myocardium in the dog. In Experiment 1, 80% of control animals died within one month, whereas 80% of treated dogs survived 37 days and 60% lived until they were sacrificed at three months. Survival was related to the development of adequate collateral circulation.

The hemodynamic findings in Experiment 2 indicate that retrograde flow can be rapidly augmented in the distal portion of occluded arteries. One must assume, therefore, that potential collateral channels exist within the heart. Like circulation elsewhere in the body, only a portion of the potential vascular bed is normally functional. Although vascular resistance in nonfunctional "closed vessels" cannot be measured, it is presumably high and, hence, a "critical opening pressure" must be applied to overcome the surface and wall tension. Increased intraluminal pressure alters the transmural pressure and increases vessel diameter.[4] In contrast to flow in rigid tubes, there is a dynamic relationship between flow, pressure, volume and calibre in distensible blood vessels. Since resistance is related to the inverse of the radius to the fourth power, resistance to flow is rapidly diminished by increments above critical opening pressure. Beyond a certain point, the resistance in small vessels becomes constant and flow is then related to the driving pressure.

In the normal heart, the principal vascular resistance is at the intramyocardial arterioles and it is here that mechanically elevated diastolic pressure exerts its major effect. Elevated perfusion pressure lowers resistance and increases flow. Coronary vascular resistance can be lowered further by diminishing myocardial tone when, during counterpulsation, left ventricular systolic pressure and systolic ejection time are reduced. In the ischemic heart, it is likely that counterpulsation particularly affects the calibre of small arteries and arterioles—those that communicate with distal branches of proximally occluded coronary arteries. Because they lack external support, epicardial vessels are potentially more responsive to counterpulsation. The diameter of small vessels increases and potential non-functioning channels open. Once collateral flow is established, it persists even after counterpulsation ceases. The pressure gradient across the ischemic bed maintains the flow, which is enhanced by a local metabolic milieu that favours vasodilatation and lessened vascular resistance.[5] The angiograms and histological studies on long-term survivors suggest that, with the passage of time, the collateral circulation increases further and that new channels accommodate to the increased flow.

Our findings support those of Wyant *et al.*,[6] who observed increased retrograde flow and a raised, ventricular fibrillation threshold after counterpulsation, and that of Goldfarb *et al.*[7] who found that myocardial oxygen tension is increased. Experiment 3 provides indirect evidence of improved perfusion of ischemic myocardium. Myocardial anaerobic metabolism was arrested and normal oxidative metabolism restored. Recently we confirmed these observations in an acute ischemia study.[8] After the left coronary artery branches were ligated, progressive left heart failure

ensued. Cardiac output, aortic pressure and coronary flow steadily declined. Concomitantly there was elevation of left atrial pressure, coronary-sinus lactate concentration and of myocardial excess lactate. Control animals died in ventricular fibrillation, but treated dogs survived. Counterpulsation supported the circulation until enhanced coronary flow and collateral circulation restored normal myocardial oxidative metabolism, and improved cardiac function and circulatory dynamics.

Summary

By experiments in the chronic, ischemic dog heart, we have demonstrated that counterpulsation can establish collateral flow to ischemic myocardium. Hemodynamic findings showed that flow in the distal portion of proximally occluded arteries was rapidly augmented by counterpulsation. This collateral flow restored the myocardial oxidative metabolism, reduced the incidence of fatal arrhythmia and myocardial infarction and prolonged survival.

Figs. 3-7 are reproduced from the *Journal of Thoracic and Cardiovascular Surgery* (**54:** 839, 1967) by permission of the publishers, The C. V. Mosby Company.

References

1. Soroff, H. S. *et al.*: Assisted circulation: II. Effects of counterpulsation on left ventricular oxygen consumption and hemodynamics, *Circulation,* **27** April (Part 2): 722, 1963.
2. Jacobey, J. A. *et al.*: A new therapeutic approach to acute coronary occlusion. I. Production of standardized coronary occlusion with microspheres, *Amer. J. Cardiol.,* **9:** 60, 1962.
3. Rosensweig, J. *et al.*: Treatment of coronary insufficiency by counterpulsation, *Ann. Thorac. Surg.,* **2:** 706, 1966.
4. Burton, A. C.: Hemodynamics and the physics of the circulation. *In*: Medical physiology and biophysics, 18th ed., edited by T. C. Ruch and J. F. Fulton, W. B. Saunders Company, Philadelphia, 1960, p. 643.
5. Berne, R. M.: Cardiac nucleotides in hypoxia: possible role in regulation of coronary blood flow, *Amer. J. Physiol.,* **204:** 317, 1963.
6. Wyant, J. D. *et al.*: The effect of postsystolic myocardial augmentation on myocardial perfusion following acute coronary occlusion, *Surgery,* **62:** 499, 1967.
7. Goldfarb, D. *et al.*: Left ventricular dynamics during diastolic augmentation after coronary artery ligation, *Surg. Forum,* **17:** 156, 1966.
8. Rosensweig, J. and Chatterjee, S.: Restoration of normal cardiac metabolism and hemodynamics after acute coronary occlusion, *Ann. Thorac. Surg.,* **6:** 146, 1968.

Résumé

Nous avons déclenché expérimentalement chez le chien une insuffisance chronique de l'artère coronaire gauche en lui appliquant des constricteurs améroïdes. Alors que 78% des chiens-témoins sont morts dans un délai d'un mois, les animaux qui avaient été traités par pression à contre-courant au 14ème jour (moment où existait une sténose d'au moins 50% de la lumière des vaisseaux), ont survécu plus de 30 jours et 60% plus longtemps encore. Le débit coronarien est tombé à 49% dès le 14ème jour et atteignait en moyenne 41% avant la mort des animaux-témoins. Chez les chiens soumis à la pression à contre-courant, une circulation rétrograde se développa dans la portion proximale, ce débit atteignant environ 89% de la circulation initiale avant constriction. La concentration en lactate du sinus coronarien monta progressivement, à mesure que se développait l'insuffisance coronarienne et, avant la pression à contre-courant, le lactate en excès était positif. Après emploi de la pression à contre-courant, la concentration en lactate déclina et le lactate en excès devint négatif. Les angiogrammes ont révélé que la circulation collatérale provenait de trois sources: l'artère coronaire droite, l'artère du septum et les branches ventriculaires antérieures diagonales naissant dans la portion proximale des constricteurs.

EXPERIMENTAL COARCTATION OF THE AORTA: HEMODYNAMICS AND HISTOLOGICAL STUDIES*

WAFIK K. HABIB, M.B., B.Ch., C.R.C.S.[C]† and
ERIC M. NANSON, M.B., Ch.B.(N.Z.), F.R.C.S.[Eng. & C], F.A.C.S.,‡
Saskatoon, Sask.

THE cause or causes of hypertension in coarctation of the aorta have been disputed for many years. Blumgart, Lawrence and Ernestene[1] and Bing *et al.*[2] suggested that it is due to the mechanical obstruction to the blood flow at the site of coarctation and through the collateral vessels. Rytand,[3] Goldblatt, Kahn and Hanzal,[4] Page,[5] Scott and Bahnson,[6] Scott *et al.*[7] and Harrison and Alton[8] all showed that a renal factor contributed to the hypertension. To date, however, no one has devised an experiment that shows that both factors might operate at the same time.

Therefore, we decided to perform experiments to assess, in one experimental preparation, both the renal and mechanical factors affecting hypertension. Hemodynamic studies were done to determine if the results of these studies would correlate with blood pressure changes. The arteries above and below the coarctation were assessed histologically.

The experimental scheme (Fig. 1) was as follows: (1) An experimental model was prepared that mimicked the congenital situation in humans (Phase I). (2) One kidney was transplanted to the neck and the contralateral kidney removed, thus placing all kidney tissue above the coarctation (Phases II and III). (3) The coarctation was resected and the aorta reconstructed three weeks after Phase III (Phase IV).

We decided that, if both the renal and mechanical factors were operating, the blood pressure should fall in a stepwise manner, first after completion of Phase III, and second after the completion of Phase IV.

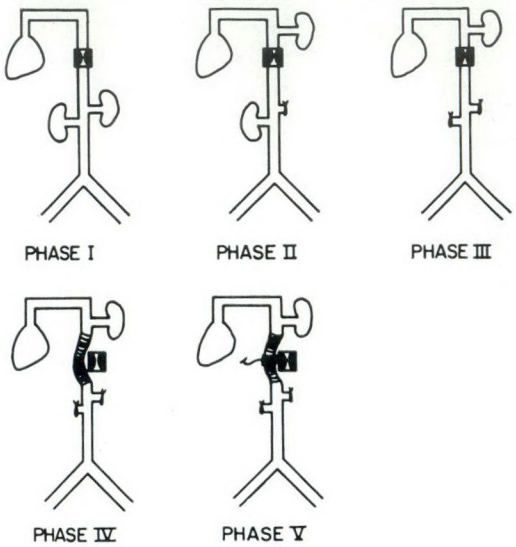

Fig. 1.—Plan of the experiment.

Finally, as an adjunct to the experiments, we hoped to recreate the coarctation by a special mechanical constricting device and so reproduce the mechanical factor associated with a return of the blood pressure level to Phase III (Phase V).

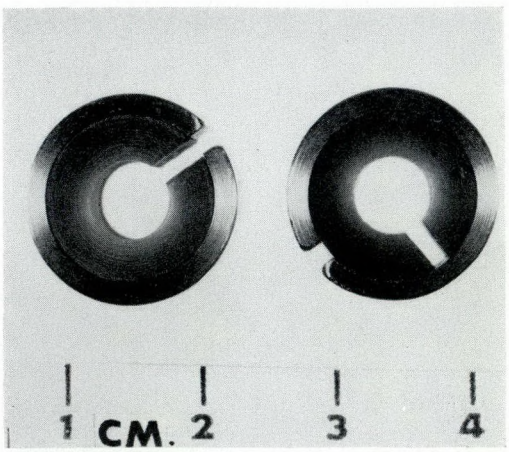

Fig. 2.—Ameroid constrictor in the open and locked positions.

*From the Department of Surgery, University of Saskatchewan, Saskatoon, Sask.

Supported in part by Medical Research Council of Canada Grant MA-1066, and in part by Surplus Earnings Pool of the Medical College, University of Saskatchewan, Saskatoon, Sask.

†Research Fellow, Department of Surgery, University of Saskatchewan.

‡Professor of Surgery, Department of Surgery, University of Saskatchewan.

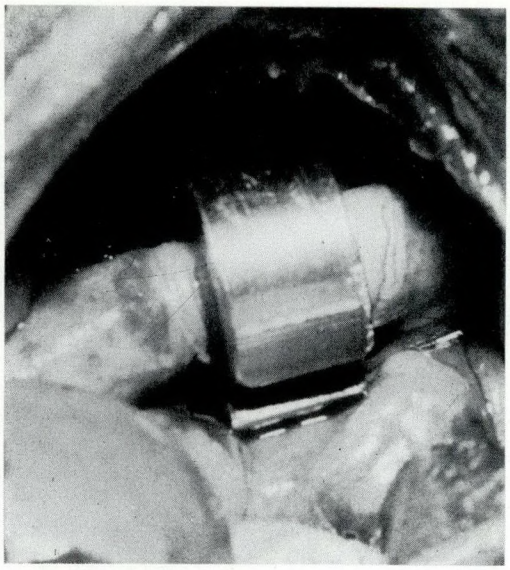

Fig. 3.—Ameroid constrictor in place around the aorta.

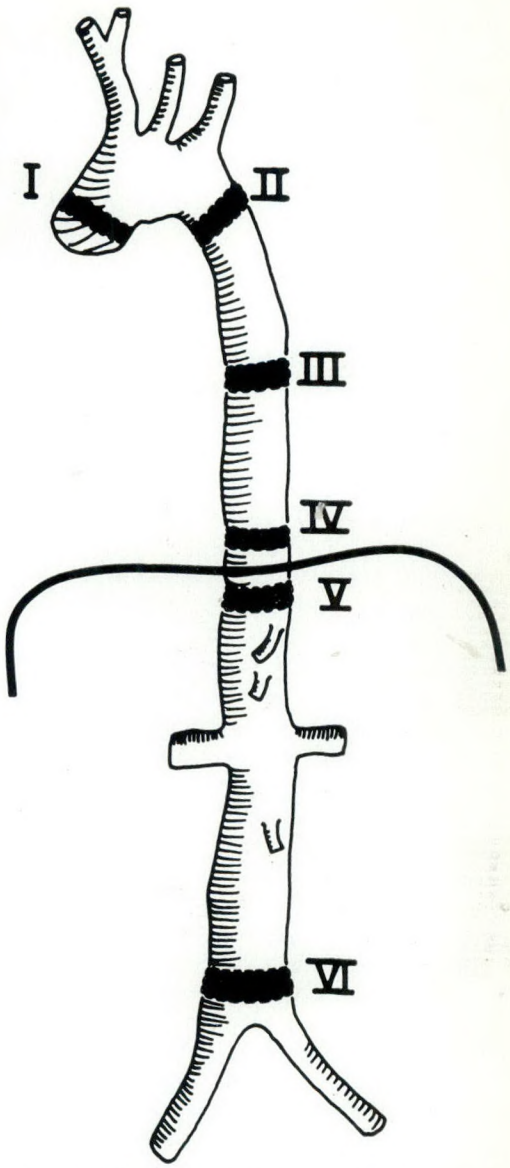

Fig. 4.—Points at which ameroid constrictors were applied on the aorta.

METHOD

Coarctations of the aorta were created in 1 to 2-month-old puppies. For this, we used ameroid constrictors[9]—bands of compressed casein hardened in formalin and surrounded by a stainless steel sleeve (Fig. 2). Through the side slit the constrictor slides around the aorta and when the metal sleeve is rotated, it locks *in situ* (Fig. 3). The casein, being hygroscopic, swells gradually over a period of two to three months. Because it is surrounded by the metal collar, it expands inwards towards the aorta, thus producing a slow but relentless constriction which, with the growth of the puppies to adult dogs, produces a satisfactory coarctation.

Constrictors were applied to the aorta at the following levels (Fig. 4): (I) the ascending aorta; (II) the descending aorta just distal to the origin of the left subclavian artery; (III) the mid-thoracic aorta; (IV) the low thoracic aorta; (V) just below the diaphragm; and (VI) below the renal arteries.

The puppies were left to grow for a period ranging from six months to two years. Then, when the dogs had been lightly anesthetized with sodium thiopentone, the cardiac outputs were calculated from the dye dilution curve by the Stewart-Hamilton method.[10, 11] Cardiac green was injected through a catheter passed down the jugular vein into the superior vena cava. Blood was withdrawn from the carotid artery at the root of the aorta by a Sage-Waters infusion pump. The blood was passed through a Waters cuvette-densitometer system, the resultant curves being inscribed on a Century oscillographic recorder. Arterial pressures were measured with a Statham strain gauge and recorded on the oscillographic recorder. At each experiment two cardiac dye dilution

curves were obtained and the average surface area of the curves was calculated using planimetry.

Cardiac output was then obtained by the following formula:

$$CO = \frac{60 \times Q}{K_1 K_2 A}$$

[Q = amount of injected dye in milligrams; K_1 = concentration value mg./l./cm.; K_2 = sec./cm. of paper; and A = curve area ($cm.^2$)].

Total peripheral resistance (TPR) was calculated in both upper and lower limbs as follows:

$$TPR = \frac{B.P. - PA \times 80}{CO} = \text{dynes/sec./cm.}^{-5}$$

(B.P. = mean blood pressure (mm. Hg); PA = right atrial pressure (mm. Hg); and 80 = conversion factor).

Aortograms were obtained by catheterizing the carotid or the femoral arteries and injecting 70% iodopyracet (Diodrast).

In the second phase of the experiment, one kidney was transplanted into the neck of the dog. The renal artery and vein were anastomosed end-to-end to the carotid artery and the jugular vein respectively. The ureter was brought to the skin as a cutaneous ureterostomy.

In most cases the other kidney was removed from the abdomen three weeks after moving one kidney to the neck. Before the contralateral nephrectomy, we obtained an intravenous urogram of the transplanted kidney. In other experiments the contralateral nephrectomy was done at the same time as the renal transplantation. The function of the transplanted kidney was periodically evaluated by estimating the blood urea and serum creatinine levels. After about three weeks we recorded the cardiac output, the blood pressure and TPR in the upper and lower limbs, with the animals under light intravenous anesthesia, in exactly the same manner as previously.

In the next phase the chest was opened again and the coarctation resected. The aorta was reconstituted with a Dacron prosthetic graft. At the end of the three weeks, we again measured the cardiac output, blood pressure and TPR.

In five dogs, when the coarctation was resected and the graft inserted, a new constricting device—a Silastic balloon in a rigid collar that could be tied around the aorta—was inserted. The balloon was connected by a small tube to a button that could be fixed under the skin (Fig. 5). By

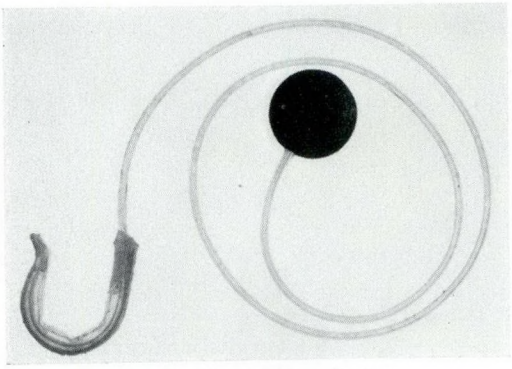

Fig. 5.—Constricting device.

injecting 3 ml. of normal saline through this button, we could distend the balloon to occlude the aorta, thus recreating the coarctation (Fig. 6).

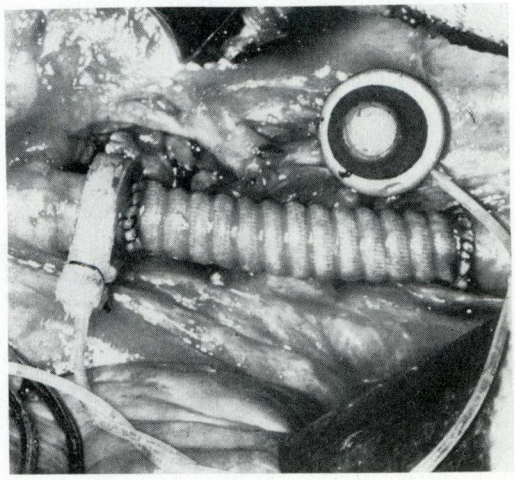

Fig. 6.—Constricting device in place.

To control renal and respiratory infections the animals were given antibiotics for varying periods of time. Also, the cutaneous ureterostomy was dilated periodically.

Results

Since 1962[12, 13] we have used this method of producing aortic coarctation in this

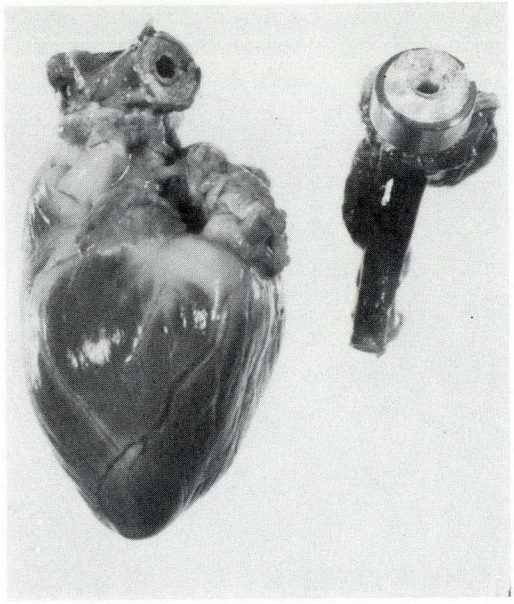

Fig. 7.—Coarctation produced in the upper descending aorta.

laboratory and it has proved most satisfactory. This method mimics the congenital anomaly in humans for the following reasons: a marked, slowly developing constriction of the aorta can be produced in the young animal and maintained as the animal grows. The aortic lumen becomes narrowed up to 85% of its original size over a three-month period (Fig. 7).

As a result of the gradual aortic constriction a good collateral circulation develops which prevents complications such as heart failure and paraplegia that may arise after acute constriction. The aortogram suggests that, when the coarctation is in the thorax, the collateral circulation is mainly through the internal mammary and the intercostal arteries and when it is in the abdominal aorta, mainly through the lumbar vessels (Figs. 8 and 9).

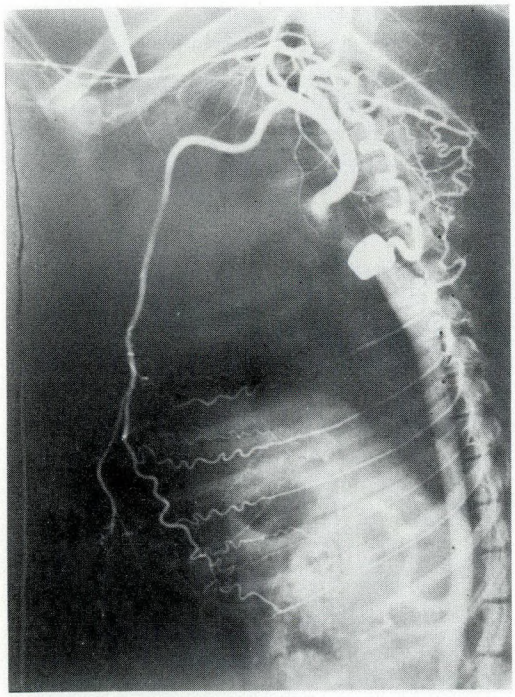

Fig. 8.—Angiogram of upper thoracic coarctation showing extensive collateral circulation.

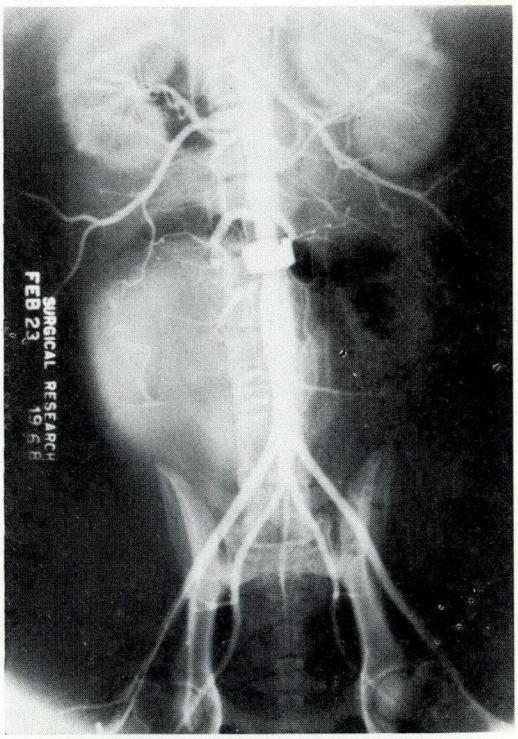

Fig. 9.—Angiogram in the presence of coarctation below the renal vessels.

Except when it was in the ascending aorta, all animals with constriction above the level of the renal arteries had hypertension with a marked pressure differential between the upper and lower limbs (Fig. 10). Constriction below the renal arteries had very little effect on the blood pressure.

In this experiment we created coarctation of the aorta at different sites in 72 puppies. Thirty-seven survived to the adult

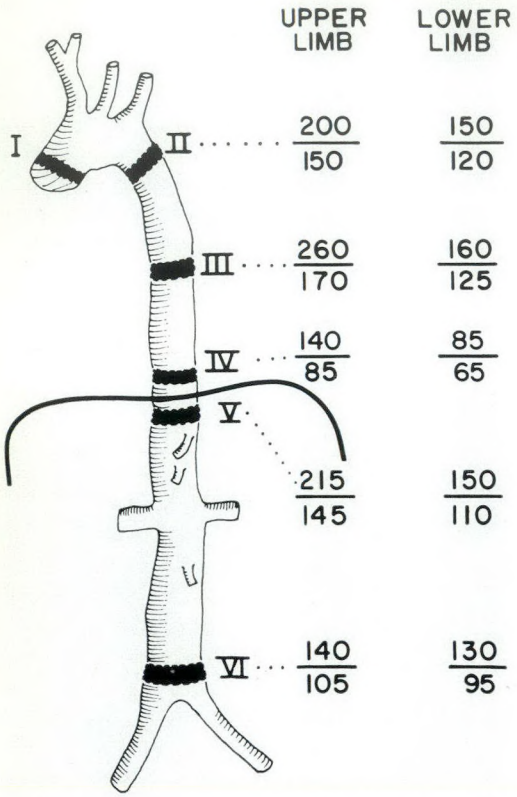

Fig. 10.—Pressures obtained by constricting various levels of the aorta.

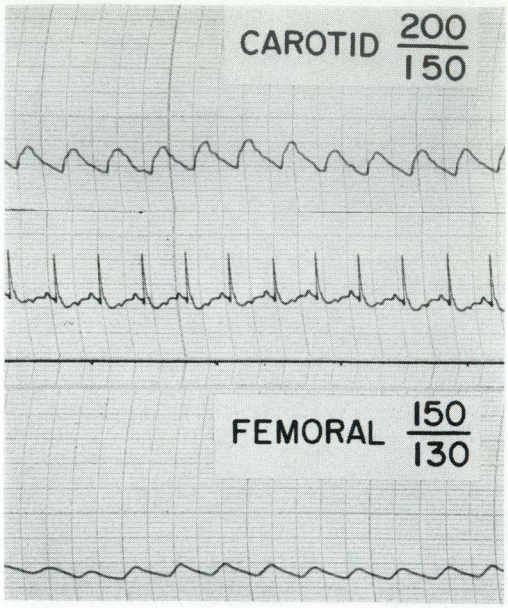

Fig. 11.—Arterial pressure tracing. A high dicrotic wave in the carotid artery compared to a low wave in the femoral artery.

stage. However, only 15 dogs lived to complete the experiment (Table I).

Four dogs were sacrificed because of their small size. In four more, renal transplantation was done with an automatic stapling device and was unsuccessful. In four dogs, coarctation was produced in the ascending aorta but three of them died suddenly after about three months due to heart failure. In only one of these dogs could we measure the blood pressure proximal and distal to the constrictor on the ascending aorta and, in this dog, the results were inconclusive because the pressures obtained were "high normal".

The three dogs that had coarctation below the renal arteries had normal blood pressures compared with normal mongrel dogs. In the other 11 dogs that completed the experiment, the blood pressure in the upper limb was as high as 240/185 mm. Hg in some and in the lower limb up to 180/150 mm. Hg.

It is interesting to note that we found hypertension in the lower limb, although the shape of the arterial pressure trace was quite different in the lower limb compared with the upper limb. The upper limb showed a dicrotic wave with a marked upstroke. In the lower limb there was no dicrotic notch and a markedly damped pressure wave (Fig. 11).

In the same 11 dogs excretory urograms of the transplanted kidney showed good function (Fig. 12). During the essential

TABLE I.—Coarctation of the Aorta. The Number of Dogs, Sites of Coarctation and Their Progress

Site of coarctation	*Number of puppies used*	*Number of dogs surviving to adult stage*	*Number of dogs completing the experiments*
Above renal arteries:			
Ascending aorta	4	1	1
Descending aorta	64	33	11
Below renal arteries	4	3	3
Total	72	37	15

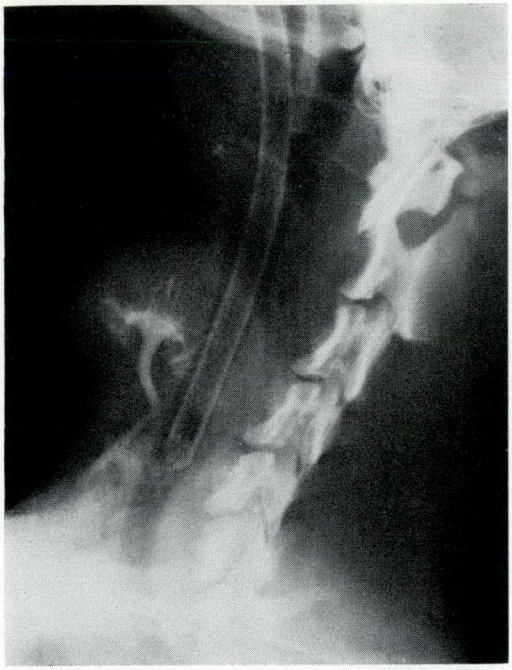

Fig. 12.—Excretory urogram of kidney transplanted in the neck.

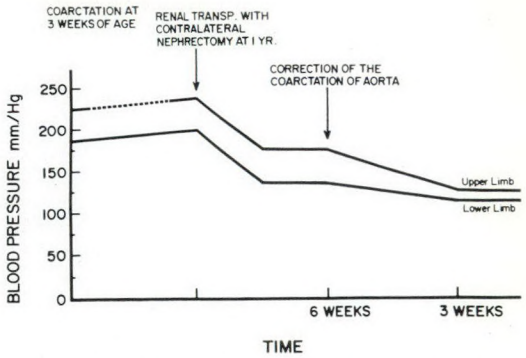

Fig. 13.—Stepwise fall of blood pressure in the upper and lower limbs after each stage of the experiment.

part of the experiment, blood urea levels varied between 30 mg./100 ml. and 60 mg./100 ml. and serum creatinine levels between 1.1 mg./100 ml. and 1.4 mg./100 ml.

After some months most of the transplanted kidneys developed pyelonephritis, renal function became impaired and blood pressure rose in some dogs. Histologically these kidneys showed varying degrees of suppuration.

Blood pressures taken three weeks after all functioning renal tissue had been transplanted above the coarctation showed that, compared with pre-transplant levels, pressures in the upper and lower limbs had fallen significantly.

After the coarctation was corrected, blood pressure fell further to within normal limits and the differential between the upper and lower limb largely disappeared. Thus, the fall in blood pressure was stepwise (Fig. 13, Table II). If renal transplantation and contralateral nephrectomy were done at the same time, there was a marked drop in blood pressure in the lower limbs (Dogs 7, 9 and 10, Table II).

We estimated cardiac output and TPR in seven dogs; the results in Dogs 7 and 9 are presented in Table III. In this experiment we could not show any correlation between cardiac output, TPR and the level of the blood pressure, and the results were so variable from one dog to another that we could draw no conclusions.

In five animals the coarctation was reproduced by the constricting device and blood pressure rose by varying degrees. However, the dogs died from congestive heart failure within a few hours or days.

TABLE II.—Blood Pressures in 11 Dogs at Different Stages

Dog number	*Pressure with coarctation*		*Kidney tissue to neck*		*After resection*	
	Upper limb	*Lower limb*	*Upper limb*	*Lower limb*	*Upper limb*	*Lower limb*
1	200/150	150/130	175/100	100/ 85	130/ 80	130/80
2	230/150	180/130	175/125	175/130	120/ 90	120/90
3	240/185	180/150	180/130	135/110	120/ 80	125/80
4	260/190	185/155	180/120	135/100	150/ 75	115/70
5	250/175	175/155	200/150	110/ 90	130/ 85	100/50
6	230/175	165/145	150/ 75	100/ 75	125/ 75	110/72
7	270/200	165/140	148/ 98	88/ 78	145/102	125/90
8	210/165	150/125	142/102	130/ 98	100/ 75	100/75
9	200/130	125/105	175/140	80/ 65	140/ 90	110/72
10	165/135	125/110	120/ 80	80/ 68	65/ 35	60/30
11	225/175	150/135	155/105	60/ 45	105/ 70	100/60

TABLE III.—Cardiac Output and Total Peripheral Resistance in Two Dogs at Different Stages

Dog number	*Stage of experiment*	*Cardiac output (l./min.)*	*Total peripheral resistance (dynes/sec./cm.$^{-5}$)*	
			Upper limb	*Lower limb*
7	With coarctation	2.20	7272	5454
	Kidney tissue to neck	1.77	4960	4060
	Coarctation resected	2.46	2923	2600
9	With coarctation	2.20	5454	3927
	Kidney tissue to neck	1.50	8267	3733
	Coarctation resected	2.20	4363	2909

Several had paraplegia. One of these dogs did not have general anesthesia, but under local anesthesia, the occluder button was exposed. An attempt to inflate the constricting balloon around the aorta precipitated immediate paraplegia which reversed as soon as the pressure was released.

In another dog, after the occluder was used, the aorta was completely occluded by thrombosis at the site of the prosthetic graft. This dog developed hypertension in the upper extremities even though all the kidney tissue was in the neck—additional evidence for the mechanical factor. After the coarctation was corrected the collateral circulatory bed collapsed rapidly.

Histological Studies

We made histological studies of the carotid arteries, the aorta above and below the coarctation, the renal arteries, and the small arteries in the sternomastoid, intercostal and rectus abdominis muscles. Sections were stained with hematoxylin and eosin, and Gomori-aldehyde-fuchsin stains. Thus, we had for comparison a group of arteries, large, medium and small, some taken from the high pressure area above the coarctation and some from the low pressure area below the coarctation.

All the arteries in the high pressure area had walls thicker than those from the low

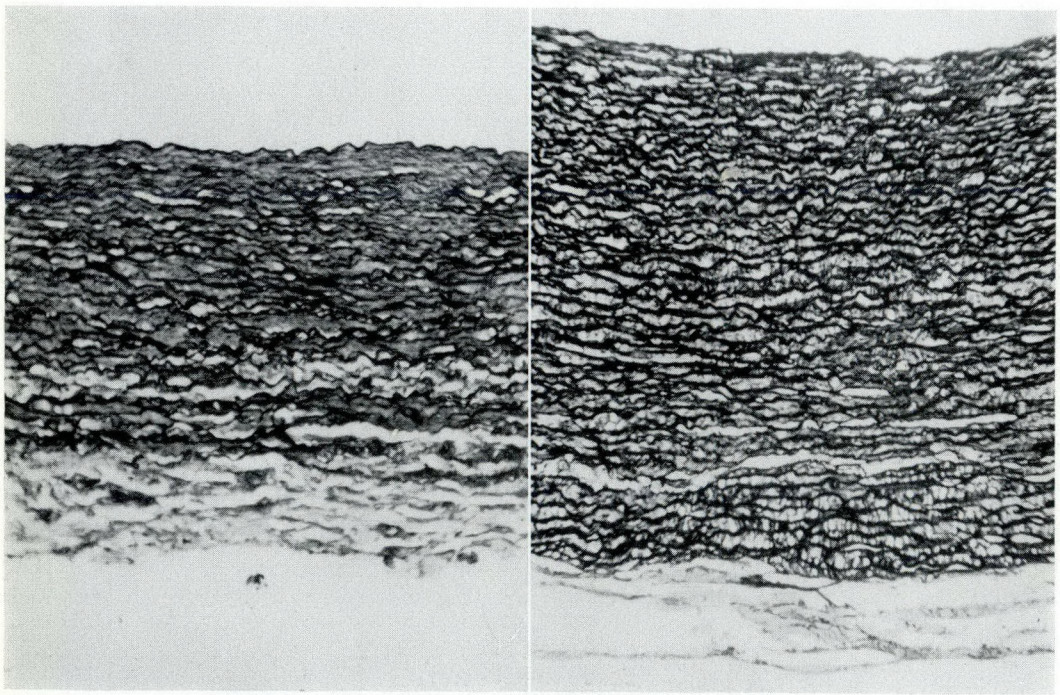

Fig. 14a **Fig. 14b**

Fig. 14.—(a) Cross-section of the aorta below the coarctation. (b) Cross-section of the aorta above the coarctation (x 180).

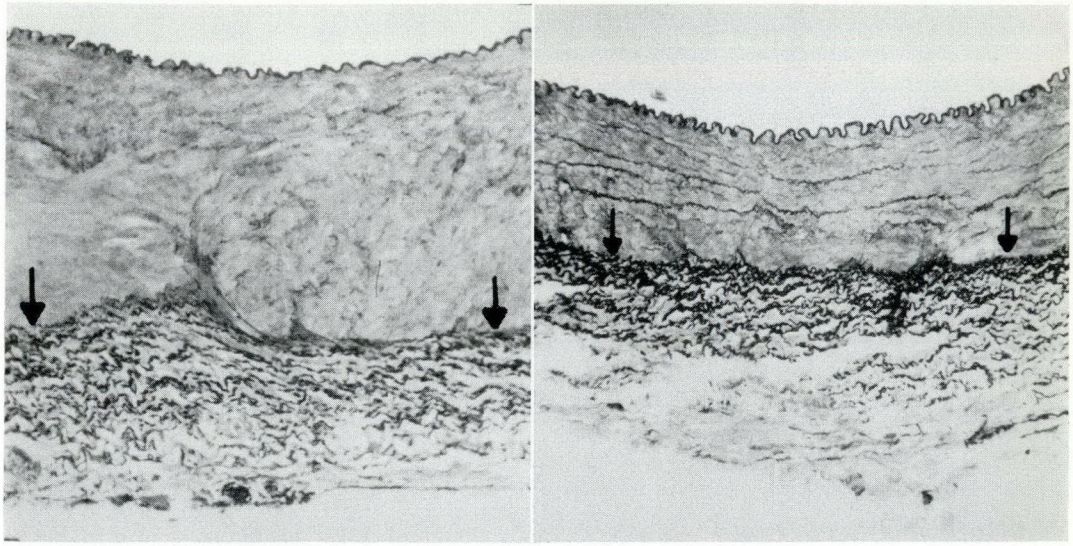

Fig. 15a Fig. 15b

Fig. 15.—(a) Cross-section of a normal renal artery. Arrows show external elastic lamina. (b) Cross-section of a renal artery from a dog with coarctation. Arrows show the external elastic lamina which is thickened when compared to (a) (original magnification x 180).

pressure area, and an increased bulk of elastic, collagen and smooth muscle tissue. However, in the aorta, the relative proportions of elastic, collagen and smooth muscle remained the same (Fig. 14). But, when the renal arteries of a normal dog and of a coarctation dog were compared, the bulk of the external elastic lamina had increased in the latter (Fig. 15). The significance of this is not immediately apparent.

The muscular layer of the small muscular arterioles in the sternomastoid muscle were much thicker than in vessels of the same size in intercostal muscles below the level of coarctation (Fig. 16).

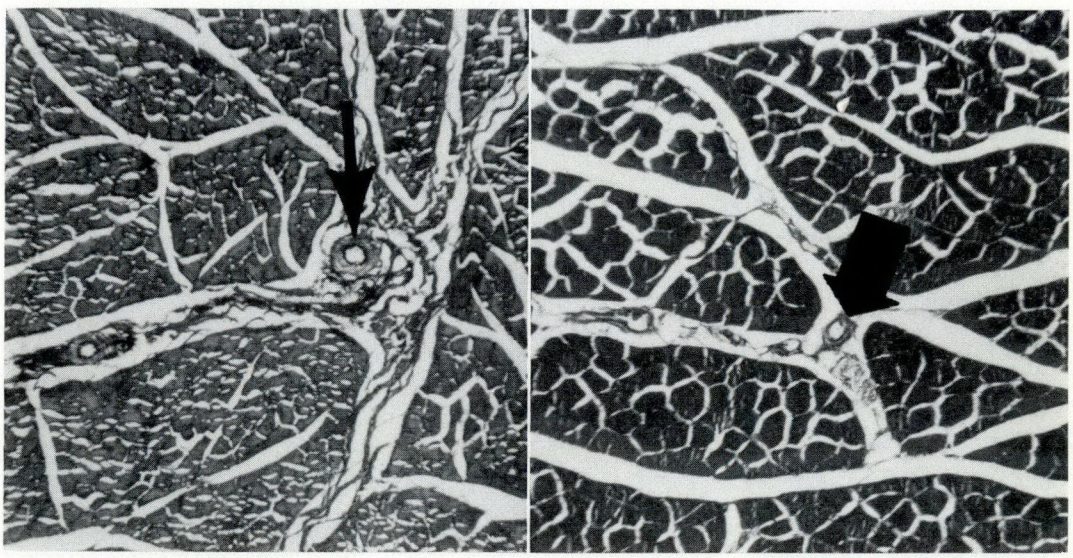

Fig. 16a Fig. 16b

Fig. 16.—(a) Cross-section of the sternomastoid muscle showing a thick-walled arteriole (arrow). (b) Cross-section of the intercostal muscle which shows a thin-walled arteriole (arrow) (x 180).

Conclusions

In this series of experiments we created in dogs coarctations of the aorta that appear to have all the characteristics of the congenital human lesion. The dogs developed marked hypertension with definite differentials in pressure above and below the coarctation.

When all renal tissue was transplanted above the coarcted area, blood pressure fell. When the coarctation was resected, the blood pressure fell further–down to normal levels. Therefore, we conclude that the hypertension associated with coarctation is due to two factors: (1) a renal factor and (2) a mechanical factor. The mechanical factor is further demonstrated by recreating the coarctation acutely and causing a return of hypertension to the level obtained in Phase III even though renal tissue was present above the new constricted area.

We have no explanation for the hypertension in the legs in both Phase I and Phase III. It might have been attributed to a renal factor, but when this was eliminated by moving all renal tissue to the neck, one would expect the hypertension below the coarctation to disappear. This did not happen.

The cardiac output and peripheral resistance in the upper and lower limbs before and after the renal tissue was moved to the neck, and after the coarctation was eliminated did not show any significant differences. We found this somewhat surprising, but cannot assert that such differences do not exist until we do more extensive studies in a greater number of dogs.

The histological studies were interesting. We compared three lots of vessels above and below the level of coarctation: (1) the aorta; (2) the small muscle vessels; and (3) the renal vessels before and after transplantation to the neck.

The aorta above was much thicker than below the coarctation, but the relative proportions of elastic, collagen and smooth muscle tissue appeared to be the same. Thus, this increase could be regarded as a work or stress hypertrophy or hyperplasia. The same could be said of the small muscle vessels. In normal animals the vessels of the sternomastoid muscle and the vessels of the intercostal muscles appeared to be comparable, but in the coarcted animal the vessels in the sternomastoid muscle which, of course, lay in the high pressure area, were definitely thickened and hypertrophied.

Sections of the renal arteries were taken when the kidney was transplanted into the neck. Then, some months later, after the renal artery had been exposed to the high pressure above the coarctation, the dog was killed and other sections were taken. The only evident change was an increase in the density and thickness of the external elastic lamina in the transplanted renal artery. It is difficult to say what significance can be attached to this increase after the artery was anastomosed with some probable proximal narrowing. However, the main objects of the experiment were achieved. We showed in a single experimental animal that, in coarctation of the aorta, both renal and mechanical factors operate in producing hypertension–thus reconciling two schools of thought.

Summary

A new method has been developed to produce coarctation of the aorta. All functioning renal tissue was transplanted above the coarctation and we studied the effect of this on blood pressure, cardiac output and total peripheral resistance. The coarctation was then resected and the effect of this on blood pressure, cardiac output and total peripheral resistance was again noted.

The results of these experiments indicate that both a renal and a mechanical cause contribute to the hypertension in coarctation of the aorta. We observed no consistent relationship between cardiac output, total peripheral resistance and blood pressure. Histologically the arteries were studied above and below the coarctation and were compared with similar arteries in normal dogs.

References

1. Blumgart, H. L., Lawrence, J. S. and Ernestene, A. C.: The dynamics of the circulation in coarctation (stenosis of the isthmus) of the aorta of the adult type; relation to essential hypertension, *Arch. Intern. Med. (Chicago)*, **47:** 806, 1931.

2. Bing, R. J. *et al.*: The surgical treatment and the physiopathology of coarctation of the aorta, *Ann. Surg.*, **128:** 803, 1948.
3. Rytand, D. A.: The renal factor in arterial hypertension with coarctation of the aorta, *J. Clin. Invest.*, **17:** 391, 1938.
4. Goldblatt, H., Kahn, J. R. and Hanzal, R. F.: Studies on experimental hypertension. IX. The effect on blood pressure of constriction of the abdominal aorta above and below the site of origin of both main renal arteries, *J. Exp. Med.*, **69:** 649, 1939.
5. Page, I. H.: The effect of chronic constriction of the aorta on arterial blood pressure in dogs; an attempt to produce coarctation of the aorta, *Amer. Heart J.*, **19:** 218, 1940.
6. Scott, H. W. and Bahnson, H. T.: Evidence for a renal factor in the hypertension of experimental coarctation of the aorta, *Surgery*, **30:** 206, 1951.
7. Scott, H. W. *et al.*: Additional observations concerning the physiology of the hypertension associated with experimental coarctation of the aorta, *Surgery*, **36:** 445, 1954.
8. Harrison, R. C. and Alton, J. D. M.: The renal factor in hypertension of experimental coarctation of the aorta, *Surg. Forum*, **5:** 146, 1955.
9. Litvak, J., Siderides, L. E. and Vineberg, A. M.: The experimental production of coronary artery insufficiency and occlusion, *Amer. Heart J.*, **53:** 505, 1957.
10. Stewart, G. N.: The pulmonary circulation time, the quantity of blood in the lungs and the output of the heart, *Amer. J. Physiol.*, **58:** 20, 1921.
11. Hamilton, W. F. *et al.*: Studies on circulation; further analysis of injection method, and of changes in hemodynamics under physiological and pathological conditions, *Amer. J. Physiol.*, **99:** 534, 1932.
12. Ty, M., Jr., Woodford, V. R. and Nanson, E. M.: An experimental study of coarctation of the aorta. Paper presented at the annual meeting of the Canadian Cardiovascular Society, Toronto, November 20-23, 1963.
13. Habib, W. K. and Nanson, E. M.: The causes of hypertension in coarctation of the aorta, *Ann. Surg.*, **168:** 771, 1968.

Résumé

L'objet de ces expériences était de découvrir la cause de l'hypertension dans la coarctation de l'aorte et de distinguer entre la cause rénale et la cause mécanique. En appliquant des constricteurs améroïdes autour de l'aorte, les auteurs ont créé expérimentalement une coarctation chez des chiots, réalisant ainsi une lésion qui imitait la lésion congénitale chez l'homme. Tous les tissus rénaux fonctionnels furent déplacés dans le cou, les plaçant de la sorte au-dessus du niveau de la coarctation. Ceci fait, la tension artérielle tomba, mais sans atteindre un niveau normal. Après résection de la coarctation, la tension artérielle tomba encore, cette fois jusqu'à une valeur normale. Quand on provoqua une seconde fois la coarctation chez quelques animaux, la tension artérielle remonta jusqu'à son niveau d'avant la résection, même si tous les tissus rénaux étaient dans le cou. On peut tirer de cette expérience la conclusion que la coarctation de l'aorte a deux causes: (1) un facteur rénal et (2) un facteur mécanique. Nous avons aussi étudié le débit cardiaque et la résistance périphérique globale mais, à aucun stade de l'expérience, nous n'avons pu déceler de changements uniformes de ces deux paramètres. Au point de vue histologique, le tissu situé au-dessus de la coarctation était plus épais qu'en-dessous, mais les proportions relatives de collagène élastine et de muscle lisse étaient les mêmes. Les petits vaisseaux musculaires au-dessus de la coarctation étaient plus épais que ceux situés en-dessous, et le muscle était hypertrophié.

TREATMENT OF RENAL ALLOGRAFTS WITH IMMUNOSUPPRESSIVE DRUGS

The authors report their experience in the past 30 months with 61 patients with living donors, 52 of whom were related and nine of whom were unrelated but histocompatible. A catheter was placed through the arterial anastomosis for local intrarenal delivery of methylprednisolone, heparin and dactinomycin. This approach was used because of the high morbidity associated with heavy initial systemic immunosuppressive therapy and the relative graft-host so-called adaptation developing with time. Initial infusion was given from one to three days and continued for 10 days in six patients. The catheter was kept patent for three weeks.

Patient survival rate was 97% and graft survival rate was 93%. The losses occurred during the first week after transplantation—in the related-donor group and in a group receiving 1 g. of methylprednisolone immediately after transplantation instead of a dose of 2 g. used in patients treated later.

A short discussion is given of possible sites of action of the locally instilled drugs, but the specific effect of each component of the solution used is not yet known.

The authors believe that a high rate of patient and graft survival has permitted a lower maintenance dose of oral immunosuppressives and short courses of large doses at an optimal time.—Kountz, S. L. and Cohn, R.: Initial treatment of renal allografts with large intrarenal doses of immunosuppressive drugs, *Lancet*, **1:** 338, 1969.

REGENERATION OF ELASTIN IN THE LIGAMENTUM NUCHAE OF THE DOG*

K. MILLS, M.B., F.R.C.S.(Edin.), M. TAKEDA, M.B., F.C.A.P., S. E. READ, M.D., M.Sc. and W. H. KIRKALDY-WILLIS, M.D., F.R.C.S.[Edin. & C], F.A.C.S., *Saskatoon, Sask.*

KIRKALDY-WILLIS *et al.*[1] studied the formation of elastin fibres in the cranial patagium of the wing of the chick embryo. The patagium, the tendon of the tensor patagii longus muscle and running from shoulder to wrist, consists of approximately 80% elastin and 20% collagen. The fine structure of these fibres described in this work is similar to that demonstrated by Greenlee, Ross and Hartman.[2] To the best of our knowledge, no one has previously studied the formation of new elastin fibres in musculoskeletal tissues in post-embryonic life. We therefore undertook to determine, by light and electron microscopy, the sequence of events in the repair of a defect in a predominantly elastin structure, the ligamentum nuchae of the dog.

MATERIALS AND METHODS

Forty-four adult, mongrel dogs were used. The ligamentum nuchae, a double band consisting of approximately 80% elastin and 20% collagen, extends at the back of the neck from the occiput to the upper thoracic spinous processes. At operation the bands of this ligament were separated and an incision was made approximately one-third of the way transversely through one band. Because of its elasticity, the cut ends pulled apart to produce a saucer-shaped defect (Fig. 1). The defect was covered with a small piece of polyethylene tubing to prevent adhesions forming to the surrounding tissues. No external splintage was used after operation.

Of the 44 dogs so treated, one was sacrificed at one day, two at three days, two at five days, six at one week, four at two weeks, four at three weeks, two at four weeks, three at five weeks, three at six weeks, one at eight weeks, one at 10 weeks, one at 12 weeks, one at 18 weeks, three at 20 weeks, two at 36 weeks, three at 42 weeks, three at 48 weeks and two at 52 weeks. This distribution was considered to be sufficient to show the early changes in the first four weeks (21 animals), the intermediate changes from 5 to 18 weeks (10 animals), and the late changes from 20 to 52 weeks (13 animals). In some dogs, the polyethylene tube had slipped to one side of the ligamentum nuchae. This occurred in three of four animals at two weeks, in one of four at three weeks, in one of two at four weeks, in two of three at five weeks, in one of three at six weeks, in the one animal sacrificed at 10 weeks and in the one sacrificed at 12 weeks. The ligament appeared to heal in the same way whether the tube was in place or not at the time of sacrifice. Portions of the defects in the ligamentum nuchae were fixed and embedded in the usual way for light and electron microscopy. The tissue was "blocked" in such a way as to show some normal ligament, the edges of the defect

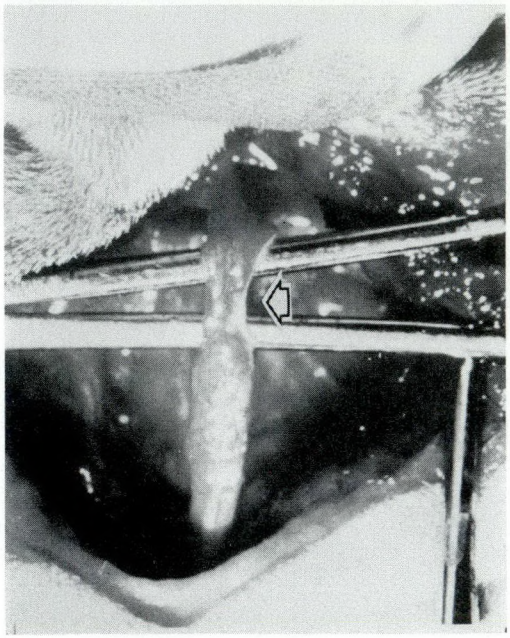

Fig. 1.—The ligamentum nuchae showing the saucer-shaped defect (arrow).

*From the Departments of Pathology and Surgery, University Hospital, University of Saskatchewan, Saskatoon, Sask.

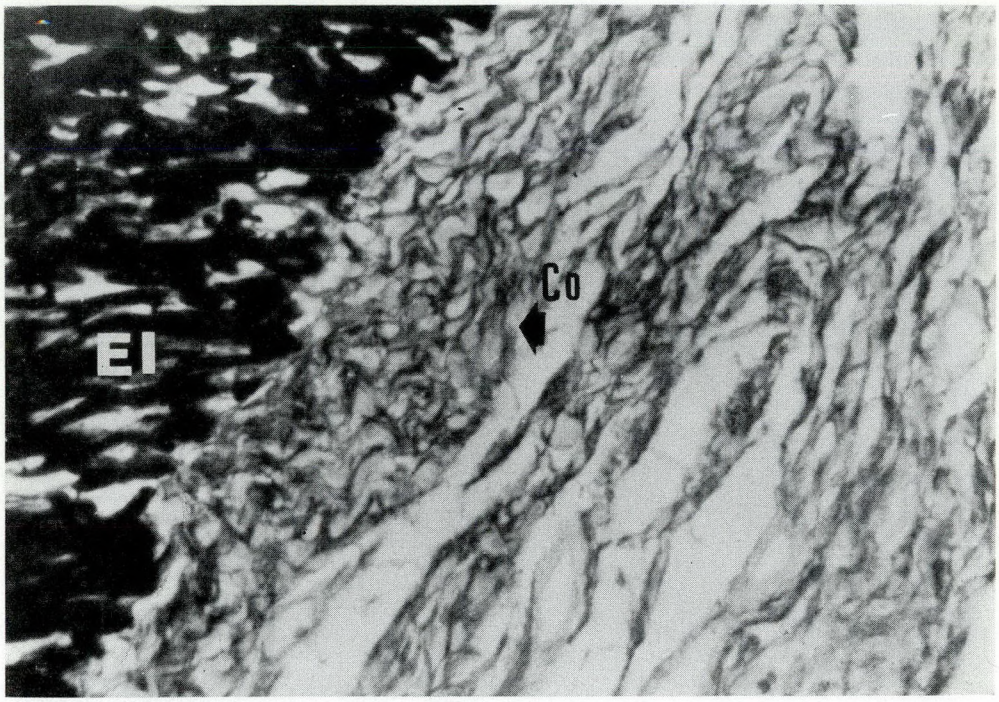

Fig. 2.—Defect at 10 weeks. The dark fibres on the left are mature elastin (El) (purple with GAF). The fine fibres on the right have the tinctorial characteristics of collagen (Co) (blue-green with GAF) (GAF x 400).

and the tissue within the defect. The sections for light microscopy were stained with hematoxylin and eosin, Gomori's aldehyde fuchsin (GAF), hematoxylin-phloxine-saffron, peracetic acid-aldehyde fuchsin-Halmi, orcinol-new fuchsin and Wilder's reticulin stain. The sections for electron microscopy were prepared by staining with lead citrate for three minutes and uranyl acetate for 10 minutes, and by staining with 2% orcein in 70% alcohol with 1 c.c. of concentrated hydrochloric acid for 10 minutes at room temperature, and with uranyl acetate for 10 minutes.

Observations

Light Microscopy

From three to seven days only fibrin and extravasated red blood cells were seen in the defect. At one week and thereafter daily till three weeks, fibroblasts and new capillaries were identified in the area. At three weeks and thereafter each week till eight weeks, thin collagen fibres were recognized. At 10 weeks the defect was almost entirely occupied by mature collagen (Fig. 2). The first evidence of new, elastin fibre production was not seen until 14 weeks. At this stage many fine fibres near the edge of the defect stained mauve with GAF. Although these fibres were only 1μ to 2μ in diameter as compared to 6μ to 8μ in mature elastin, their general appearance and particularly their uniformity of diameter strongly suggested elastin fibres. Their tinctorial reactions were more like elastin than collagen. This mauve staining was seen in every section from 14 to 20 weeks. At 20 weeks the specimens stained with GAF showed an increased number of mauve fibres (Fig. 3). These fibres were larger in diameter than those seen at 14 weeks. The cells in the area had the appearance of fibroblasts. At 30 weeks the diameter of the new elastin fibres had increased to approximately one-half that of mature fibres and they stained with the same intensity as mature fibres (Fig. 4). Although new elastin was formed in the defects, there was still relatively much more collagen than in a normal ligamentum nuchae. At 42 weeks the appearance of the defect was virtually the same

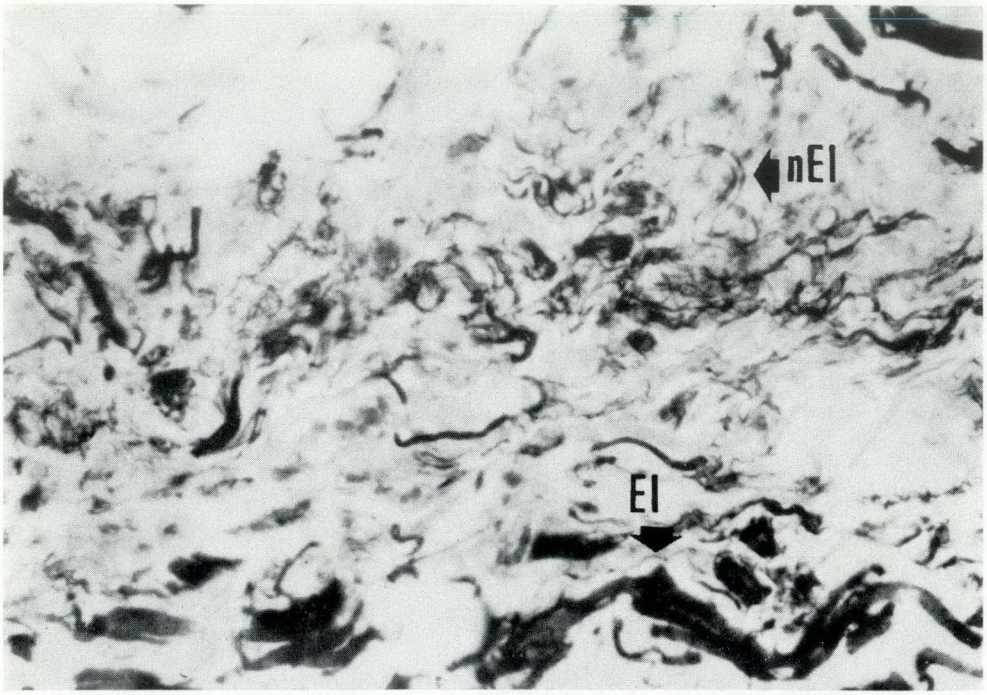

Fig. 3.—Defect at 20 weeks. The thick, dark fibres are mature elastin fibres (El) from the edge of the defect. The fine, dark fibres are newly formed elastin fibres (nEl). They have almost the same tinctorial qualities as the large fibres (GAF x 250).

as at 30 weeks, but the content of elastin fibres was increased (Fig. 5). At one year there was slightly more elastin, but there was still a marked preponderance of col-

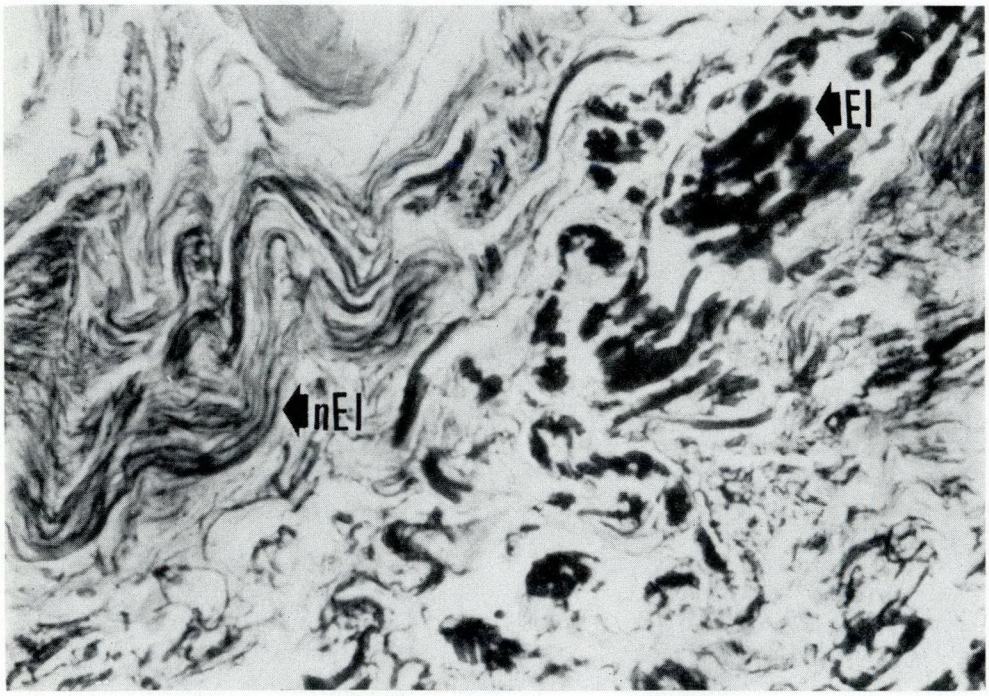

Fig. 4.—At 30 weeks. Numerous, dark, thick, mature fibres (El) are seen. Equally numerous, dark, thin, new elastin fibres (nEl) are seen (GAF x 250).

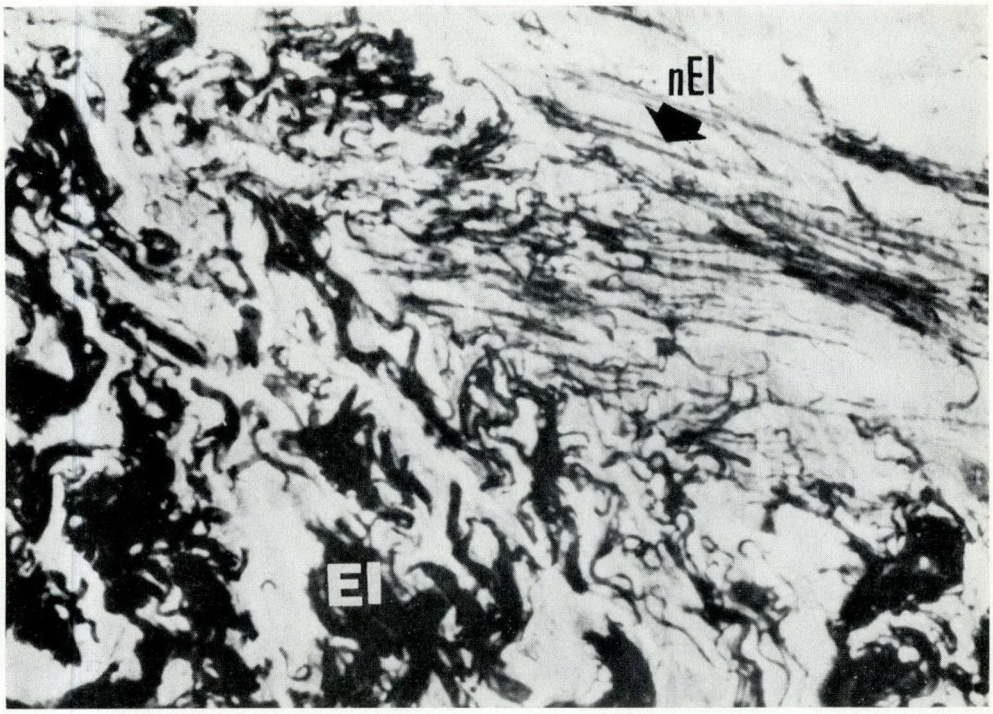

Fig. 5.—At 42 weeks, the new elastin fibres (nEl) are much larger than those in Fig. 4. They stain purple with almost the same intensity as the mature elastin (El) (GAF x 250).

lagen. Thus, in 13 biopsy series from 20 to 52 weeks, the appearance was of gradually maturing elastin in slowly increasing amounts.

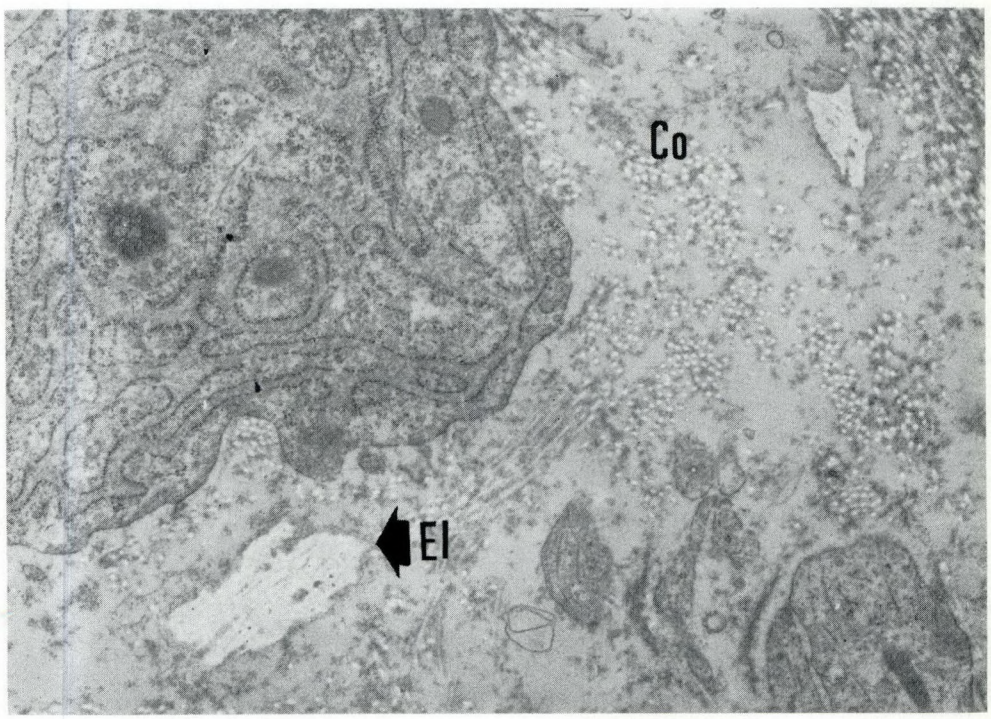

Fig. 6.—Electron photomicrograph at 21 days. In the extracellular space are two portions of elastin fibres (El) and numerous collagen fibres (Co) (x 6840).

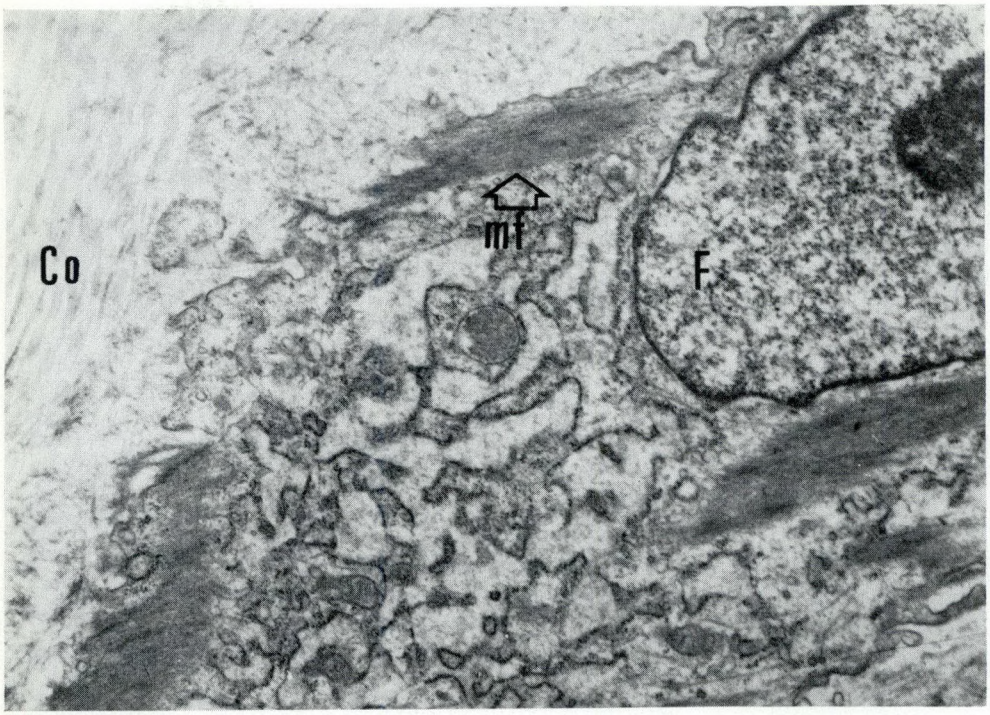

Fig. 7.—Electron photomicrograph at six weeks. Numerous intracellular aggregates of microfibrillae (mf) are seen. The fibroblast (F) contains markedly distended endoplasmic reticulum (x 4500).

Electron Microscopy

In the specimen obtained at three weeks numerous collagen fibres and a few elastin fibres were identified in association with fibroblasts which had a well-defined endoplasmic reticulum (Fig. 6). The collagen was recognized by its typical 640 to 700 A periodicity. In the six-week specimen, we saw further evidence of new elastin fibre formation—portions of young elastin fibres characterized by closely aggregated groups of microfibrillae with occasional areas of amorphous material scattered throughout them. This material was also stained with orcein and the amorphous material became electron-dense. A fibroblast was seen in the field with dilated saccules of rough-surfaced endoplasmic reticulum indicating that it was actively synthesizing protein. In the specimen obtained at six weeks, several aggregates of microfibrillae were seen. These appeared to be inside the cytoplasm of fibroblasts (Fig. 7). In the 30-week specimen, the sections contained numerous elastin fibres. These were extracellular and surrounded by collagen fibres. There was more electron-lucent material among the microfibrillae. In specimens stained with orcein this amorphous material was electron-dense (Fig. 8). In the 38-week specimen the portions of elastin fibres seen had the appearance of mature elastin (Fig. 9). Large areas of electron-lucent amorphous material were seen with a few fine longitudinal striations, mainly at the periphery.

Discussion

The process we observed was slow and gradual but we are satisfied that this experiment gave a reliable picture of the way in which healing took place after defects were made in the ligamentum nuchae. In retrospect it might have been better not to have covered the defect with polyethylene tubing. In some instances the tubing became displaced but there appeared to be no difference in healing whether the tubing was in place or not.

The healing of the defect by fibrin formation, fibroblastic infiltration and deposition of collagen fibres orientated at random proceeded along normal lines but appeared to be much slower than anticipated. There

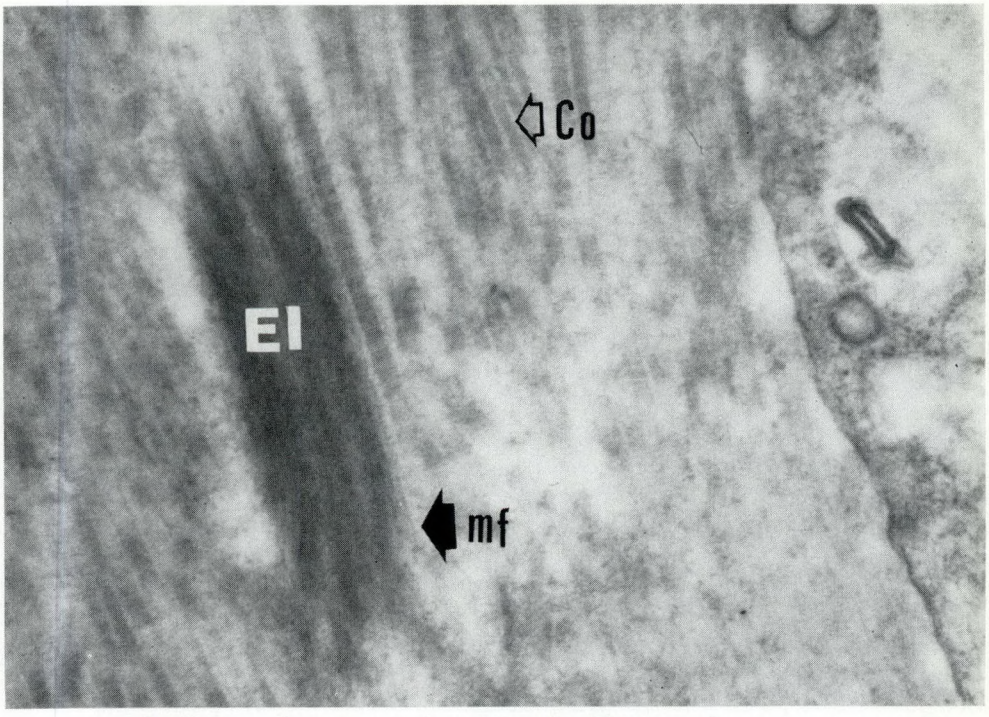

Fig. 8.—Electron photomicrograph at 30 weeks. Elastin in the sections is more abundant. This photomicrograph taken at a higher magnification and stained with orcein shows an area of aggregated microfibrillae (mf) with an increased amount of electron-dense material among them. This is a young elastin fibre (El). Collagen fibres (Co) with the typical cross-banding can be seen in many parts of the field (orcein x 22,500).

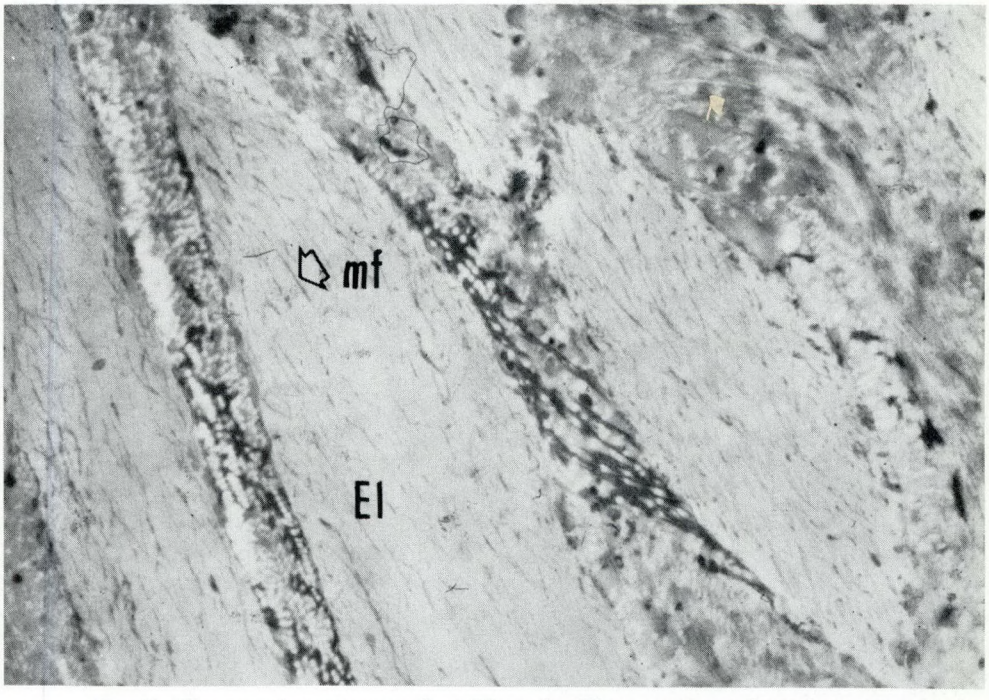

Fig. 9.—Electron photomicrograph at 38 weeks. Three portions of nearly mature elastin fibres are seen. These consist mainly of electron-lucent amorphous material with fine longitudinal striations that are the microfibrillae (mf) which are almost completely masked (x 6840).

was very little, if any, collagen deposition before three weeks. This was surprising. Because the ligamentum nuchae is a predominantly elastic structure (80% elastin fibres), we expected to observe a more rapid and complete formation of elastin fibres. The first evidence of immature elastin fibres was not seen until six weeks after operation; from then on, the process of maturation was slow. This process and an increase in the number of elastin fibres formed proceeded slowly but steadily up to one year. Thirty weeks after the operation the diameter of the new elastin fibres was approximately one-half normal. From then until one year there was little change. It is particularly surprising that elastogenesis was so slow and incomplete when one considers how rapidly this process proceeds in the repair of arterial-wall defects. This latter process has been demonstrated convincingly by Florey *et al.*;[3] they observed that the pseudointima formed in prostheses inserted in arteries contained both collagen and elastin fibres. Buck[4] demonstrated the same process after double ligation of arteries. We have seen this process in the femoral artery of the dog after the intima and internal elastic lamina had been stripped away; within two months a new internal elastic lamina had formed. Taylor, Baldwin and Hass[5] have shown that the same changes take place after the rabbit aorta is frozen.

Studies on the formation of elastin fibres in the cranial patagium of the wing of the embryo chick[1] might lead one to expect that a process occurring so rapidly in the embryo would also take place in adult animals. It might be argued that the organism has a marked ability to produce elastin fibres in many of its tissues in embryonic life but that many tissues and organs lose this ability shortly after birth. However, Jellinek[6] demonstrated that elastin fibres proliferated in the skin after x-irradiation. In our laboratory Kitegawa[7] observed the same process in the wall of the urinary bladder and the urethra after deep x-ray therapy for carcinoma of the cervix. Sams, Smith and Burk[8] demonstrated that elastosis occurred after exposure to ultraviolet light. Furthermore, Murphy and McPhee[9] and Finlayson, Smith and Moore[10] demonstrated that elastin fibres increased in skin, tendon, lung and bone in chronic renal acidosis. It is clear therefore that, under certain conditions—even grossly abnormal ones—fibroblasts can deposit elastin fibres in tissues other than heart and major blood vessels.[3]

As stated above, Florey *et al.*[3] demonstrated that new elastin fibres formed in the lining of arterial prostheses. We found no reference in the literature to the formation of new elastin fibres in skin healing. Lindsay and Birch[11] described in considerable detail the way in which skin wounds heal and referred to the deposition of collagen fibres but did not mention elastin. Janzen,[12] in this laboratory, demonstrated varying numbers of new elastin fibres in the healing dermis after operation in man. He has also shown that there is a preponderance of elastin in chronic, infected skin wounds in the sole of the foot. Birch and Lindsay,[13] describing the fate of tendon grafts in the chicken, do not mention the formation of elastin fibres, although these fibres form in chronic renal acidosis.[9, 10]

Therefore, what environmental factors stimulate elastogenesis and which of these operate in the ligamentum nuchae of the dog? Lelkes and Karmazsin,[14] working with chick embryo cultures of heart and aorta, showed that elastin fibres only formed when the tissue cultures were associated with pulsating heart cultures. In the chick embryo Murakami[15] showed that elastin fibres developed in the aorta shortly after the embryonic heart had begun to pulsate. These observations suggest that rhythmic movement and pulsation are essential factors in the formation of elastin fibres. Certainly such pulsation is normally present in arteries, being transmitted by the action of the heart to the arterial wall. Animals with long necks, such as the dog, sheep and horse, have a well-developed elastic ligamentum nuchae. Man, pig and cat have shorter necks and this structure is composed almost entirely of collagen fibres. Animals with long necks submit their necks to rhythmic movement in feeding and other activities but possibly this is too slow and too irregular to influence elastin-fibre formation in post-fetal life.

Haust, More and Movat[16] postulated two types of repair: vascular and avascular. They believe that avascular repair takes place most frequently in the walls of atherosclerotic arteries, which seems somewhat paradoxical until one considers that the inner one-third of the wall of most arteries is not supplied by the vasa vasorum. Perhaps elastin fibres are only laid down by fibroblasts or by smooth muscle cells in areas where the oxygen tension and the pH are low. This theory receives corroboration from the work of Jellinek[6] on x-irradiation of the skin where the avascularity produced by radiation appears to stimulate the fibroblasts. Murphy and McPhee[9] and Finlayson, Smith and Moore[10] demonstrated that elastin fibres increased in a number of tissues in chronic renal acidosis, presumably because this decreased pH and oxygen tension. In these experiments, for several weeks after the defect was made in the ligamentum nuchae, the area, first filled with fibrin and then with collagen fibres, was relatively avascular. This is somewhat surprising if only avascularity, with low pH and oxygen tension, stimulates elastogenesis.

Black-Schaffer, Grinstead and Braunstein[17] showed that the endocardium of large mammals contains a large amount of elastin, and attributed this to a rapid increase in the mural tension during the growth and development of these animals. The large amount of elastin in the endocardium of the human heart in secondary endomyocardial fibroelastosis may be explained in the same way, this process being dependent on congenital abnormalities of the heart. From these considerations it appears that the main factors leading to elastogenesis are rhythmic movement and pulsation, and mural tension with a tendency to dilatation—environmental factors that are present in the heart and arteries but absent from the ligamentum nuchae. In other words, when tissue is avascular and subjected to rhythmic activity, the fibroblast is stimulated to form elastin fibres. When the tissue is relatively vascular and not subjected to rhythmic activity, this cell forms collagen. Under the conditions of these experiments, the ligamentum nuchae appears to lie between these two extremes; repair takes place through the formation of approximately 80% collagen fibres and 20% elastin fibres. The ligamentum flavum in man is not dissimilar to the ligamentum nuchae in the dog. It is interesting to speculate whether the repair of defects in the ligamentum flavum, such as those made during the exploration of an intervertebral disc, takes place in the same way as it does in the ligamentum nuchae of the dog. This possibility we hope to investigate when we re-explore an intervertebral disc that has already been explored and can examine a ligamentum flavum in which a defect was made earlier.

Summary

In defects in the ligamentum nuchae of the dog elastin regenerated but to a limited extent. According to electron microscopic observations, the events in fibre production follow the same sequence in regeneration as in embryogenesis. We saw no morphological distinction between the cells that produced elastin and those that produced collagen. We have discussed the factors that may favour elastogenesis.

We wish to thank the Canadian Arthritis and Rheumatism Society and the Medical Research Council of Canada for their generous support. We are also grateful to Mrs. W. J. Kao, M.Sc., for her technical assistance and to Mr. Hans Dommasch, R.B.P., F.B.P.A., A.R.P.S., of the Medical Photography Department, University of Saskatchewan, for his help and advice.

References

1. Kirkaldy-Willis, W. H. *et al.*: Elastogenesis in the cranial patagium of the wing of the chick, *Canad. J. Surg.*, **10:** 348, 1967.
2. Greenlee, T. K., Jr., Ross, R. and Hartman, J. L.: The fine structure of elastic fibers, *J. Cell. Biol.*, **30:** 59, 1966.
3. Florey, H. W. *et al.*: The pseudointima lining fabric grafts of the aorta, *Brit. J. Exp. Path.*, **42:** 236, 1961.
4. Buck, R. C.: Intimal thickening after ligature of arteries, an electron-microscopic study, *Circ. Res.*, **9:** 418, 1961.
5. Taylor, C. B., Baldwin, D. and Hass, G. M.: Localized arteriosclerotic lesions induced in aorta of juvenile rabbit by freezing, *Arch. Path. (Chicago)*, **49:** 623, 1950.
6. Jellinek, S.: Proliferation of elastic fibres after x-irradiation, *Lancet*, **2:** 1192, 1962.
7. Kitegawa, T.: Personal communication.

8. Sams, W. M., Jr., Smith, J. G., Jr. and Burk, P. G.: The experimental production of elastosis with ultraviolet light, *J. Invest. Derm.*, **43:** 467, 1964.
9. Murphy, K. J. and McPhee, I.: Tears of major tendons in chronic acidosis with elastosis, *J. Bone Joint Surg. [Amer.]*, **47A:** 1253, 1965.
10. Finlayson, G. R., Smith, J. G., Jr. and Moore, M. J.: Effects of chronic acidosis on connective tissue, *J. A. M. A.*, **187:** 659, 1964.
11. Lindsay, W. K. and Birch, J. R.: Thin skin healing, *Canad. J. Surg.*, **7:** 297, 1964.
12. Janzen, H. K.: Personal communication.
13. Birch, J. R. and Lindsay, W. K.: Histochemical studies of the fate of autologous digital flexor tendon grafts in the chicken, *Canad. J. Surg.*, **7:** 454, 1964.
14. Lelkes, G. and Karmazsin, L.: Development of elastic elements in tissue cultures, *Acta Morph. Acad. Sci. Hung.*, **5:** 149, 1955.
15. Murakami, H.: Personal communication. Otemae Hospital for Crippled Children, 9 Hoensaka-cho, Higashi-ku, Osaka, Japan, 1965.
16. Haust, M. D., More, R. H. and Movat, H. Z.: The role of smooth muscle cells in the fibrogenesis of arteriosclerosis, *Amer. J. Path.*, **37:** 377, 1960.
17. Black-Schaffer, B., Grinstead, C. E., II and Braunstein, J. N.: Endocardial fibroelastosis of large mammals, *Circ. Res.*, **16:** 383, 1965.

Résumé

Les chercheurs ont créé des anomalies en forme de soucoupe dans une bande des ligaments de la nuque chez le chien. Cette structure anatomique est composée de 80% d'élastine et de 20% de collagène. En vue d'étudier le processus de guérison de ce défaut, et, en particulier, le mode de formation des fibres d'élastine, les animaux ont été sacrifiés à intervalles réguliers, variant d'une semaine à un an. Pendant les premières semaines, la lacune se remplissait uniquement de fibrine. Après un mois, il y avait dépôt de fibres de collagène. Il fallut attendre six mois pour apercevoir des fibres d'élastine au microscope optique, plus tôt cependant au moyen du microscope électronique. Au bout d'une année, la lacune était comblée de tissus composés de 80% de collagène et de 20% d'élastine.

Les auteurs ont comparé la régénération de l'élastine dans les ligaments postérieurs de la nuque, dans la tunique élastique interne après endartériectomie et la cicatrisation qui s'opère dans d'autres tissus, la peau et les tendons notamment. Dans diverses conditions cliniques et expérimentales, les facteurs importants de stimulation de l'élastogénèse sont les mouvements répétés et rythmiques d'une structure; l'anoxie et le faible pH résultent de l'absence de vascularisation.

Il ressort de ces expériences que, dans toute étude des plaies et de leur cicatrisation après un traumatisme ou un processus inflammatoire, le chirurgien devrait étudier non seulement le dépôt de réticuline et de collagène, mais aussi celui de l'élastine.

TREATMENT OF HEPATIC COMA BY PURIFICATION IN HETEROLOGOUS LIVER

It has been shown experimentally that an isolated pig liver can be kept alive and functioning by perfusion with human blood. Subsequent investigations have shown that pig liver can be connected to the blood circulation of a patient suffering from hepatic insufficiency. Two different circuits have been described: a simple one, where the blood leaves the femoral artery, circulates through a heat exchanger and enters the liver through the portal vein. The blood then leaves the liver via the cannulated vena cava, enters a reservoir and is infused into the patient's femoral vein through a filter and debubbler. The second, more complicated system incorporates an oxygenator and a second (recirculation) pump in the circuit which allows oxygenation of the extracorporeal liver. A third modification is the separate cannulation and perfusion of the hepatic artery. The extracorporeal system and the technique for preparing the pig liver are presented in detail. The indications for use of an extracorporeal isolated pig liver are as follows: (1) hepatic coma following acute hepatitis (viral or toxic), (2) coma associated with portocaval anastomosis, and (3) selected cases of hepatocellular insufficiency in severe cirrhosis of the liver.

The authors have treated four patients and report a satisfactory decrease of the level of bilirubin and ammonia in the blood. Immunological reactions due to the perfusion of the pig liver have not been observed, but there are other complications such as a bleeding tendency. In the authors' opinion, the results reported in the world literature have been mediocre. They believe that there is an excessive enthusiasm for this method and that the main value of extracorporeal liver perfusion might be additional insight into the pathophysiology of liver disease which this treatment provides.—Leger, L. *et al.*: Traitement du coma hépatique par épuration dans un foie hétérologue, *J. Chir. (Paris)*, **97:** 161, 1969.

FREE OVARIAN AUTOGRAFTS WITHIN THE UTERUS*

H. PATRICK DORR, M.D., C.M., F.R.C.S.[C], F.A.C.S., A. HABRE, M.D. and DAVID S. KAHN, M.D., *Montreal, Que.*

Disease and occlusion of the fallopian tubes are major causes of female sterility. Plastic operations to restore tubal patency are seldom successful because the impairment of tubal function is usually permanent. As an alternative the ovary could be placed within the uterus, completely bypassing the problems of tubal patency and function. Previously, in rabbits, we studied the survival of pedicle ovarian autografts with preserved blood supply.[1] We now describe studies of free ovarian autografts in the uterine cavity. Skin was used as the control autograft and the renal cortex was used as the control graft site.

Materials and Methods

The experimental animals, mature female rabbits, weighed between 5 lb. and 10 lb. To rule out reproductive tract abnormalities, all had previously had at least one litter. They were fed standard rabbit chow with supplemental leafy vegetables and were housed in individual cages.

During operations, we used intravenous pentobarbital anesthesia, skin shave and preparation with benzalkonium chloride solution, sterile instruments, clean but nonsterile gloves and 4-0 nylon and 5-0 catgut sutures. After operation, the rabbits received intramuscular penicillin-streptomycin immediately. For intrauterine grafts a midline lower abdominal incision was used. Both ovaries were excised. At the upper end of each uterine horn, the endometrium was exposed through an incision

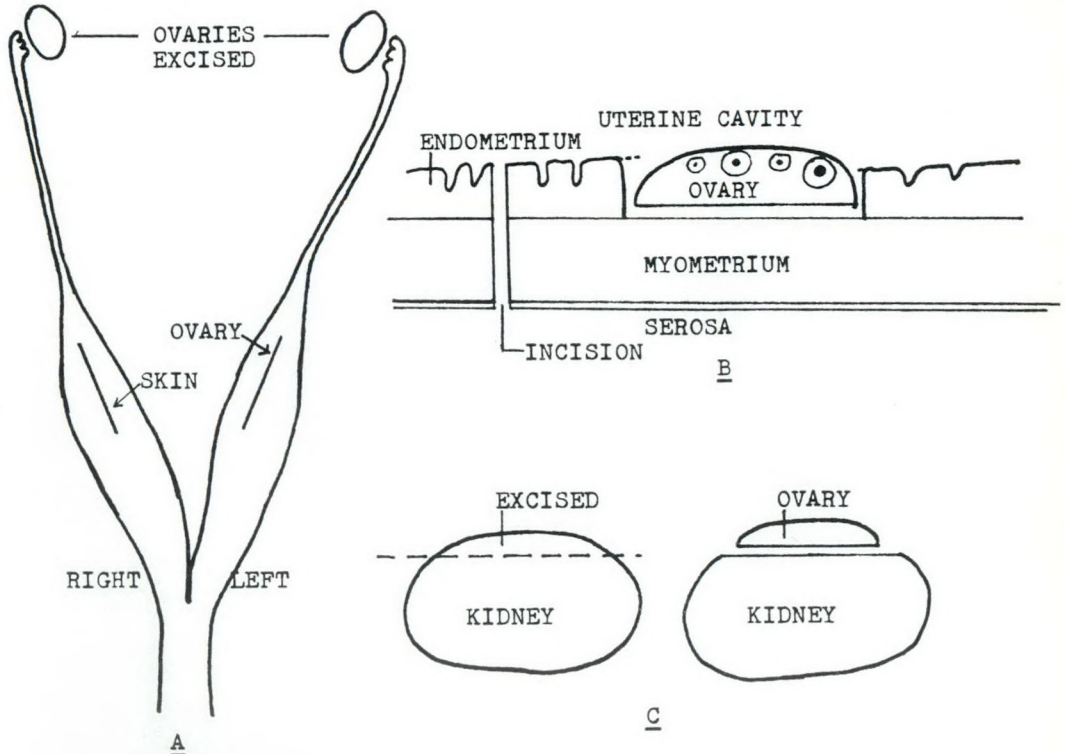

Fig. 1.—The operative techniques. (A) Rabbit uterus. Graft sites for ovary and skin in left and right uterine horns respectively. (B) Intrauterine graft site, cross-section. (C) Renal cortex graft site.

*From the Departments of Obstetrics and Gynecology, and Pathology, St. Mary's Memorial Hospital, and the Department of Pathology, McGill University, Montreal, Que.

Supported by Medical Research Council of Canada Grant MA-2389.

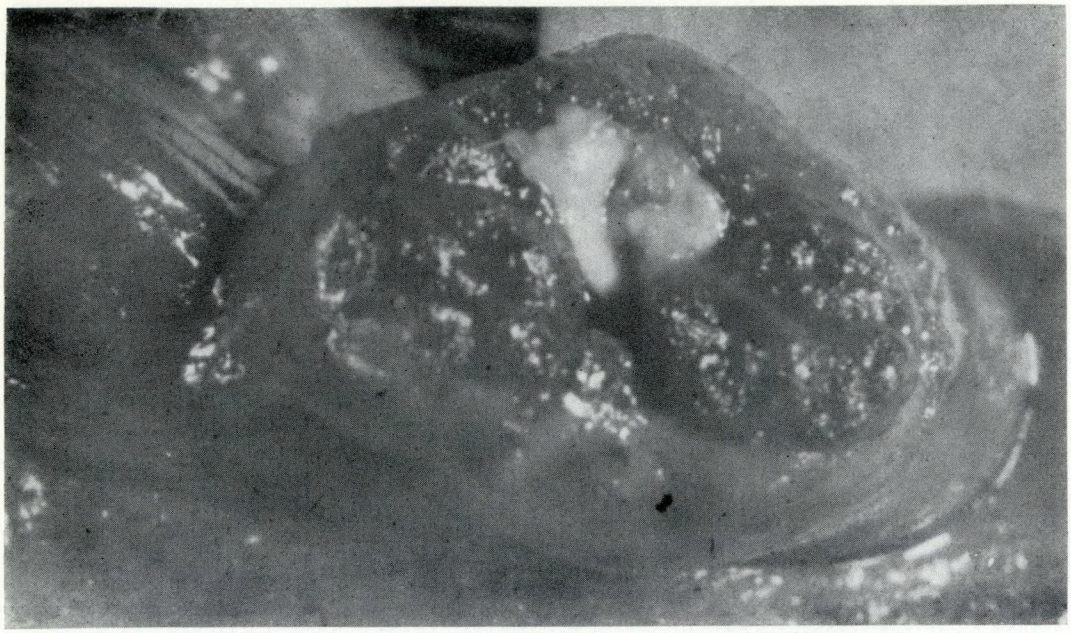

Fig. 2.—Left uterine horn. The endometrium has been excised and the ovarian graft sutured to the myometrium.

in the antimesometrial side. Approximately 1 sq. cm. full-thickness endometrium was excised preparing a graft site. By means of interrupted catgut sutures, a thin slice of ovarian tissue was fixed to the graft site in the left uterine horn. In a similar fashion a full-thickness skin graft from the inner surface of the rabbit's ear was placed in the right horn. The uterine incisions were closed (Figs. 1A, 1B and 2).

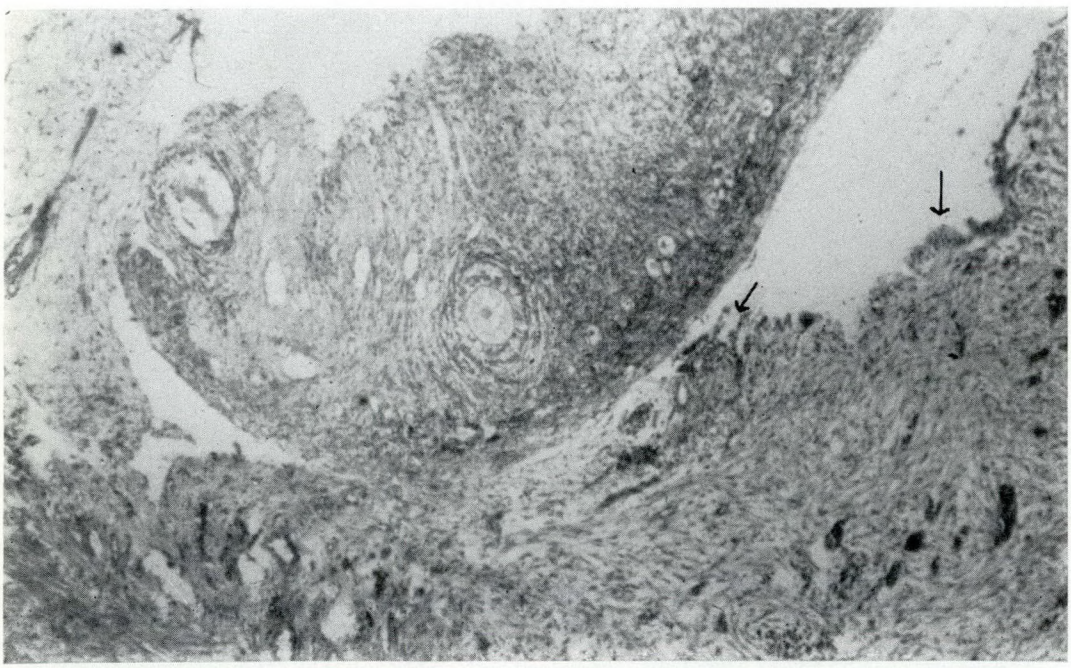

Fig. 3.—Photomicrograph of inverted ovarian graft to the uterus, two stages. Regeneration of the endometrium (arrows) 24 hours after the second stage interferes with graft vascularization (H & E, original magnification x 25).

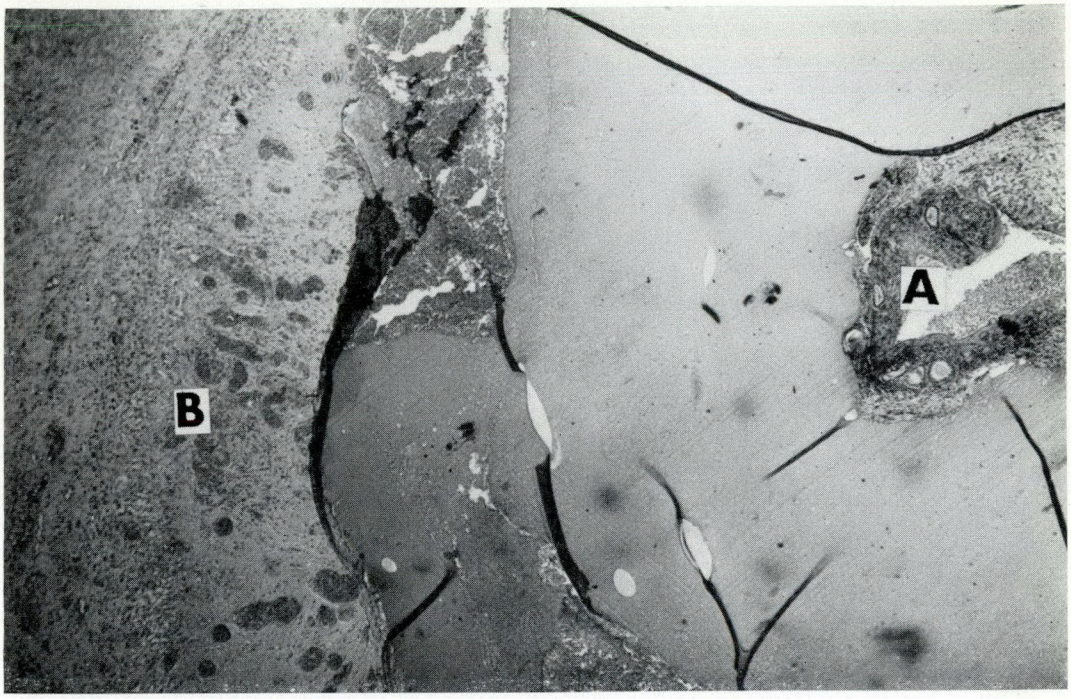

Fig. 4.—Photomicrograph of ovarian graft attached with adhesive. "Fixed" ovarian tissue (A) is separated from necrotic endometrium (B) by a wide area of unabsorbed hyaline adhesive (H & E, original magnification x 25).

We also studied several variations of the intrauterine grafting technique. In some animals the grafts were done as a two-stage procedure. At an initial laparotomy the endometrium was excised to prepare the graft site. At repeat laparotomy four days later, the ovaries were excised and the slice of ovary transplanted. In another variation the ovarian grafts were inverted, that is, the slice of ovary was placed on the myometrium with the normally external germinal epithelial surface directly against the site (Fig. 3). In other animals the grafts were attached to the myometrium with a gelatin-resorcinol-formaldehyde adhesive[2, 3] rather than with sutures (Fig. 4). Some rabbits were treated with medroxyprogesterone acetate, 10 mg. intramuscularly, four days before grafting.

For grafts to the renal cortex, we used the technique developed by Wheeler, Corson and Dammin[4] for splenic and liver autografts in mice. The left kidney was palpated and exposed transabdominally through an overlying oblique incision in the left flank. The kidney was freed from the perirenal fat and exteriorized through the incision. A rubber-shod clamp was placed on the renal pedicle. A slice of renal cortex, approximately 1-cm. square and 0.1-cm. thick, was excised. Bleeding from the cut surface was allowed to stop spontaneously. The left ovary was excised through the kidney incision and the right ovary through a separate small incision in the right lower quadrant. A slice of ovary, approximately 0.1-cm. thick was placed on the cut surface of the kidney without sutures. The clamp was removed from the renal pedicle. The renewed oozing did not dislodge the graft and ceased after a further 10 minutes. The kidney was then returned to its normal position, taking care not to disturb the graft. In a similar fashion, full-thickness skin grafts from the inner surface of the rabbit's ear were transplanted to a bed in the renal cortex (Figs. 1C and 5).

The following groups were studied: Group 1a—ovarian grafts to uterus, one stage; Group 1b—ovarian grafts to uterus, one stage, with medroxyprogesterone; Group 2a—ovarian grafts to uterus, two stages; Group 2b—ovarian grafts to uterus,

Fig. 5.—Ovarian graft to the renal cortex. A clamp is on the renal pedicle.

two stages, with medroxyprogesterone; Group 2c—ovarian grafts to uterus, two stages, with ovary inverted; Group 2d—ovarian grafts to uterus, two stages, with adhesive; Group 3—ovarian grafts to renal cortex, one stage; Group 4—skin grafts to uterus, one stage, with medroxyprogesterone; Group 5a—skin grafts to uterus, two stages; Group 5b—skin grafts to uterus, two stages, with medroxyprogesterone; Group 5c—skin grafts to uterus, two stages, with adhesive; Group 6—skin grafts to renal cortex, one stage.

Some of the rabbits with ovarian grafts on the renal cortex received human chorionic gonadotrophin, 100 to 500 units intravenously, one to four days before the animals were killed.

The rabbits were killed at 30 and 60 days after transplantation. Those that died or developed gross infection of the abdominal incision or peritoneal cavity or other postoperative complications were eliminated from the series. Sixty-one were suitable for evaluation; there was a minimum of five rabbits in each group. The uteri and left kidneys were removed and fixed in formalin. Suitable tissue blocks were chosen for histological examination. Tissue sections were stained with hematoxylin and eosin.

Results

Graft survival was based on histological criteria. The following were used for

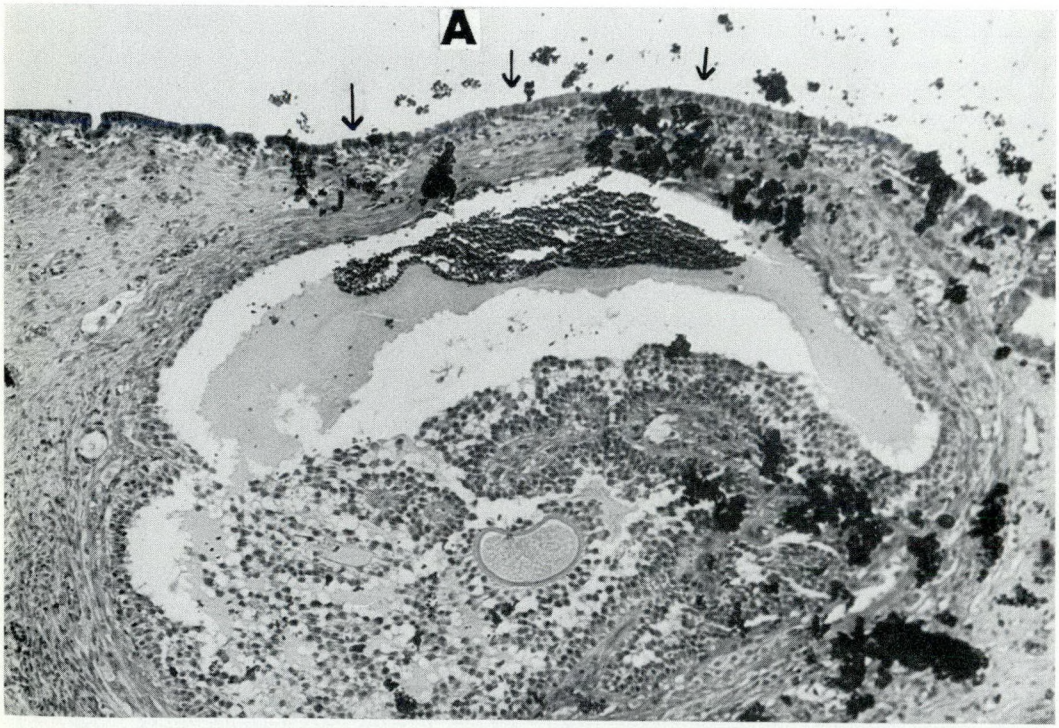

Fig. 6.—Photomicrograph of ovarian graft to the uterus. Developing follicle is separated from the uterine cavity (A) by a thin layer of endometrium (arrows) (H & E, original magnification x 63).

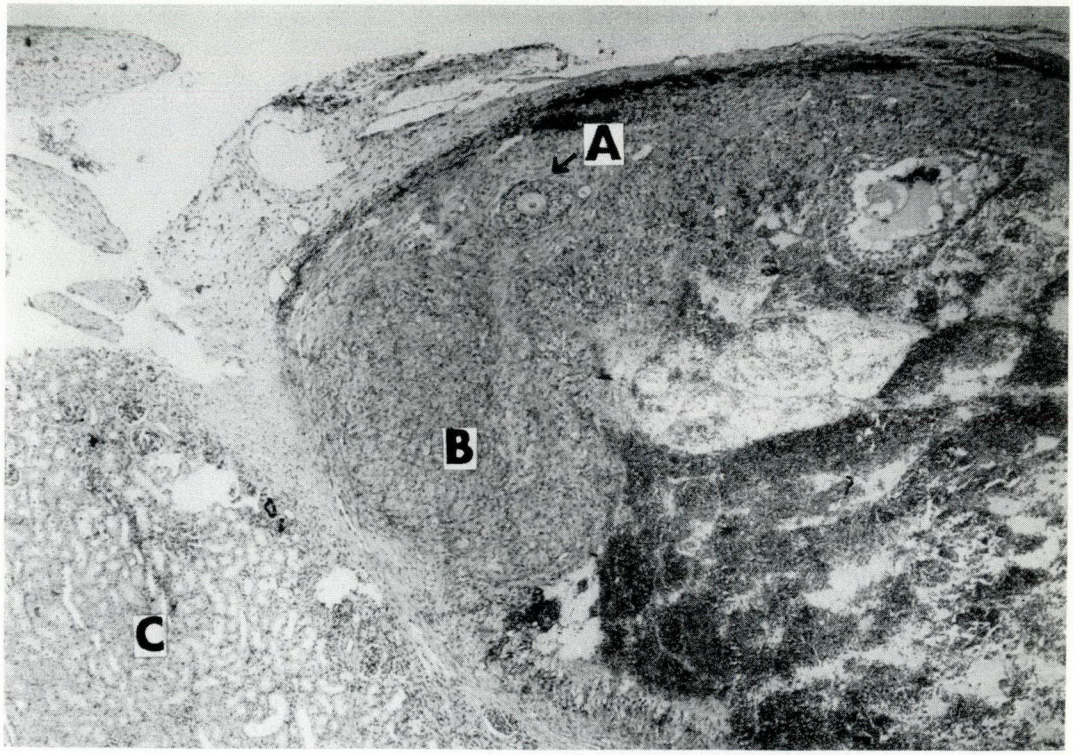

Fig. 7.—Photomicrograph of ovarian graft to the renal cortex showing ovum and follicle (A), corpus luteum (B) and renal cortex (C) (H & E, original magnification x 25).

ovarian-transplant survival: ovarian stroma, follicles, ova and corpora lutea (Figs. 6 and 7). The presence of stratified squamous epithelium indicated a successful skin graft (Fig. 8).

The results of ovarian grafts are sum-

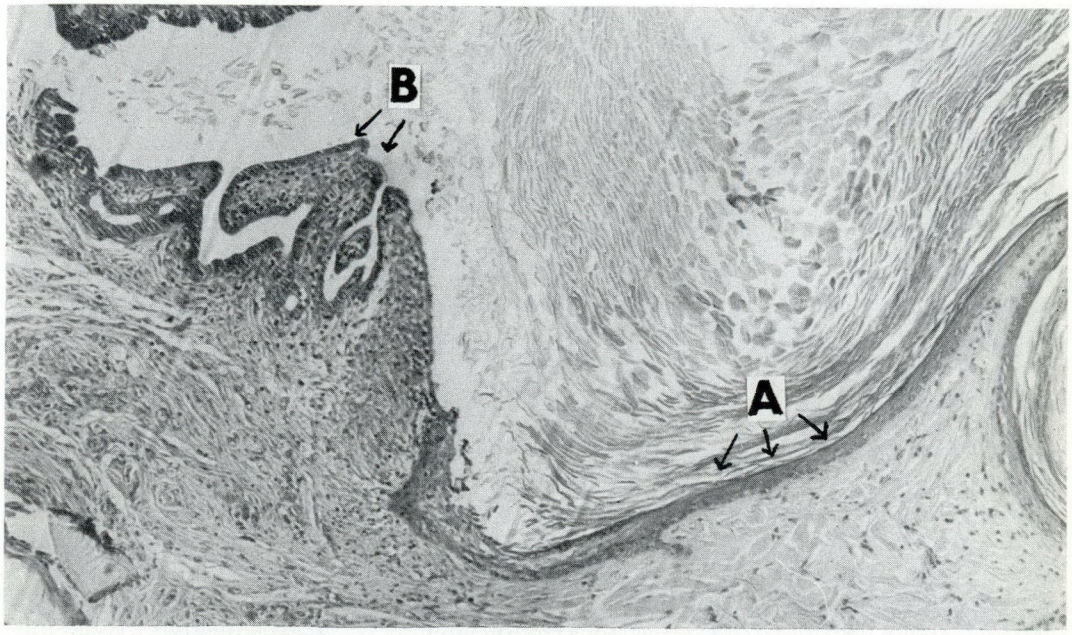

Fig. 8.—Photomicrograph of skin graft to the uterus shows squamous epithelium (A) in continuity with columnar epithelium of the endometrial surface (B) (H & E, original magnification x 63).

TABLE I.—Free Ovarian Autografts

Group	*Graft technique and variations*	*Number of animals*	*Survival of stroma*	*Survival of follicles/ova/ corpora lutea*
1a	To uterus, one-stage	16	16	2
1b	To uterus, one-stage, with medroxyprogesterone	7	5	1
1	1a + 1b	23	21 (91%)	3 (13%)
2a	To uterus, two-stage	7	2	0
2b	To uterus, two-stage, with medroxyprogesterone	5	2	1
2c	To uterus, two-stage, with ovary inverted	8	4	1
2d	To uterus, two-stage, with adhesive	6	0	0
2	2a + 2b + 2c + 2d	26	8 (31%)	2 (8%)
3	To renal cortex, one-stage	12	10 (83%)	8 (67%)

marized in Table I and of skin transplants in Table II. When ovarian transplants to the uterus were done as a one-stage procedure (Group 1), the stroma survived in 21 of 23 animals and follicles/ova in three.

TABLE II.—Free Skin Autografts

Group	*Graft technique and variations*	*Number of animals*	*Survival of skin*
4	To uterus, one-stage, with medroxyprogesterone	7	6 (86%)
5a	To uterus, two-stage	11	7
5b	To uterus, two-stage, with medroxyprogesterone	5	2
5c	To uterus, two-stage, with adhesive	6	0
5	5a + 5b + 5c	22	9 (41%)
6	To renal cortex, one-stage	5	5 (100%)

With ovarian transplants as a two-stage procedure (Group 2) stroma survived in 8 of 26 animals and follicles/ova in two. Ovarian transplants to the renal cortex as a one-stage procedure (Group 3) showed stromal survival in 10 of 12 animals and follicles/ova in eight. When skin was transplanted to the uterus as a one-stage procedure (Group 4) squamous epithelium survived in six of seven animals. Skin transplants to the uterus as a two-stage procedure (Group 5) showed that the squamous epithelium survived in 9 of 21 animals. In skin transplants to the renal cortex (Group 6) squamous epithelium survived in all five animals. When the rabbit received chorionic gonadotrophin before being killed, ovarian grafts to the renal cortex contained corpora lutea.

At the graft sites of myometrium and renal cortex, we saw only mild to moderate non-specific reactions of inflammatory cells and connective tissue proliferation. The ovarian transplants to the uterus were always covered by a layer of endometrium which separated the ovarian tissue from the uterine cavity (Fig. 6). By contrast, skin grafts to the uterus remained exposed to the uterine cavity. The endometrium made no attempt to cover these transplants and the squamous epithelium of the graft was in direct continuity with the endometrial surface columnar epithelium (Fig. 8). The uterine cavity was often stenosed at the graft site and the cavity above this area was distended with serous fluid. The grafts attached by gelatin-resorcinol-formaldehyde adhesive mainly persisted. However, the fragments of ovary and skin appeared to have been preserved by the formaldehyde rather than to represent viable tissues. In the graft site, they were surrounded by an intense inflammatory reaction and marked tissue necrosis. Large zones of the adhesive remained unabsorbed. From histological evidence, we could not assess the survival of these grafts although probably they were not viable (Fig. 4).

Discussion

Two techniques were used to transplant the ovary to an intrauterine location: first, we introduced the whole ovary into the uterine cavity with a pedicle containing the ovarian artery and vein;[1] second, we

placed a free graft of ovarian tissue against the uterine wall (myometrium) from which the graft must derive its blood supply. The advantages of the free graft are: (1) it avoids potential interference with a vascular pedicle and the difficult vascular anastomoses of small ovarian vessels that would be required with homografts of ovarian tissue. (2) The uterine incision can be completely closed to avoid a uterine-wall defect. (3) With it, portions of ovary can be used that are salvaged from operations for severe adnexal disease.

A free autograft survives through wound healing between the tissues of the graft and the host site. The graft must revascularize from the host site early enough to prevent necrosis of the graft tissue. Homografts, with the added problems of immunological rejection, cannot be attempted until a technique can be developed that succeeds with autografts.

The results in Group 3—ovarian grafts to the renal cortex—suggest that all constituents of the ovary will survive autotransplantation. Ovarian stroma survived in 83% of rabbits and follicles/ova in 66%. That the transplanted follicles/ova retain function is indicated by the corpora lutea that developed in the transplanted ovary in Group 3 rabbits that received chorionic gonadotrophin.

With one-stage intrauterine grafts, ovarian stroma or skin survived quite well (91% and 86% respectively) whereas the more specialized structures, follicles and ova, survived in only 13%.

We attempted to improve the survival of these essential structures by varying the technique, hoping that the two-stage procedure would provide a bed of young granulation tissue that would allow more rapid revascularization of the ovarian graft. However, in the four days between stages, although granulation tissue had filled in the graft bed, it was already being covered by a layer of regenerating endometrial epithelium (Fig. 3). This layer probably interfered with graft nutrition because survival of both ovarian stroma and skin was less in this group than in the one-stage procedure.

Other variations in technique were tried, but these did not improve graft survival. We inverted the ovarian graft to place the follicles and ova, which are directly below the surface germinal epithelium, immediately adjacent to the graft site and thus as close as possible to the blood supply. Some rabbits were pre-treated with medroxyprogesterone four days before grafting in an attempt to improve uterine vascularity and inhibit myometrial contractility. Neither of these variations improved the survival of the special structures (follicles and ova), which are essential for reproductive and endocrine function.

The results of this study indicate that ovarian follicles and ova are less likely to survive the anoxia of free transplantation than ovarian stroma and skin. However, using a favourable graft site such as the renal cortex, it is possible to obtain a high rate of survival of follicles and ova. Although the intrauterine site is unfavourable for these specialized structures, their occasional survival indicates that the technique is feasible. If the intrauterine ovarian graft was covered by a layer of endometrium, it probably would not interfere with rupture of a developing follicle and release of the ovum into the uterine cavity (Fig. 6). The factors that determine survival of these specialized structures when they are transplanted to the uterus are still unknown. Revascularization of the graft appears to be critical. Although the variations in procedure in this study, intended to improve graft vascularity, were unsuccessful, we are now studying other techniques in an endeavour to improve the results.

Summary

Rabbits were used to study the survival of free ovarian autografts to an intrauterine location and to the renal cortex. In grafts to the kidney there was good survival of follicles and ova (66%), but when transplanted to the uterus these specialized structures survived poorly (13%). Less specialized tissues, ovarian stroma and skin, showed much better survival following intrauterine transplantation. Variations in the technique of transplantation did not improve the survival of follicles and ova in the free intrauterine ovarian autografts.

REFERENCES

1. DORR, P., ABED, M. AND KAHN, D. S.: Ovarian transplantation to an intrauterine location: survival of ovarian pedicle autografts, *Canad. J. Surg.*, **11:** 230, 1968.
2. COOPER, C. W. AND FALB, R. D.: Surgical adhesives, *Ann. N.Y. Acad. Sci.*, **146:** 214, 1968.
3. BONCHEK, L. I. AND BRAUNWALD, N. S.: Experimental evaluation of a cross-linked gelatin adhesive in gastrointestinal surgery, *Ann. Surg.*, **165:** 420, 1967.
4. WHEELER, H. B., CORSON, J. M. AND DAMMIN, G. J.: Transplantation of tissue slices in mice, *Ann. N.Y. Acad. Sci.*, **129:** 118, 1966.

RÉSUMÉ

Chez le lapin, les auteurs ont étudié la survie d'autogreffes d'ovaires libres transplantés dans la cavité intra-utérine et dans le cortex rénal. Dans les greffes au rein, 66% des follicules et des ovules ont survécu, mais seulement 13% de ces structures spécialisées ont survécu à leur transplantation dans l'utérus. Des tissus moins spécialisés, notamment le stroma ovarien et la peau ont joui d'une plus longue survie après transplantation intra-utérine. Les auteurs même en modifiant la technique de la transplantation, ne sont pas parvenus à prolonger la survie des follicules ovariens et des ovules dans les autogreffes intra-utérines d'ovaires libres.

AVULSION OF THE INTEGUMENTS OF PENIS AND SCROTUM

The authors used a tunnelled graft from the skin of the internal surface of the thigh to replace the skin of the penis and scrotum after complete avulsion of the genital skin in a 42-year-old agricultural worker. His left testicle had been completely torn from the cord. The right testicle had been completely denuded of skin. All skin covering the genital organs had been avulsed. The loss of the penile skin extended from 2 cm. from the base of the penis to the glans, with only a small amount of prepucial tissue remaining. The glans, however, was intact.

The authors first tied the stump of the cord of the left testicle at the external inguinal ring. The right testicle was placed into the subcutaneous pouch in the anterior perineal region. There was no tension on the spermatic cord with the testicle in this position.

A tunnel of skin from the internal surface of the left thigh was then constructed, leaving only a minimum of the fatty tissue on the deep surface of the graft. A Foley catheter was placed through the urethra and then the penis was inserted into the tunnel. The remaining collar of the prepuce was sutured circumferentially to the inferior part of the detachment.

This basic repair and the construction of the skin graft was followed 15 days later by liberation of the flap. At a third intervention, the complete mobilization of the penis was accomplished. The patient was able to leave the hospital two months and 10 days after the accident.

The cosmetic effect of the plastic repair was satisfactory. The sensitivity of the penile skin was normal. The testicle was viable and did not cause the patient any distress.

Four months after the accident the patient was able to resume his sexual activities. There was, however, a sclerotic lesion that caused the penis to deviate to the left. Plastic repair involved resection of all of the fibrous tissue at the base of the penis on the side of the left inguinal fold. Ten days later the patient was able to leave hospital.

The final results were satisfactory. The patient's sexual activity was considered to be as good as it was before the accident. The sensitivity of the replaced skin was "absolutely perfect". This was believed to be an important factor in the restoration of normal erection.

Anatomic studies confirm that the innervation of the skin of the superior internal surface of the thigh is a particularly erotic zone and identical to that of the skin of the penis and scrotum. The innervation is assured by the genitocrural nerve and by a genital branch of the abdominal genital nerve. Each of these nerves sends branches to the penis, scrotum and the superior internal surface of the thigh.

The authors, in removing the cutaneous flap, took special care to preserve the innervation and not to remove too much of the fatty subcutaneous tissue.—Vives, P., Veyssière, C. and Laude, M.: Avulsion complète des téguments du pénis et du scrotum, *Lille Chir.*, **23:** 203, 1968.

EFFECTS OF SLOW INFUSION OF ENDOTOXIN IN THE DOG*

N. A. RETY, M.B., B.S., M.Sc.(Surg.), F.R.C.S.[C]† and
C. M. COUVES, B.A., M.D., F.R.C.S.[Edin. & C], F.A.C.S.,‡ *Edmonton, Alta.*

As is well recognized, endotoxin liberated from the cell wall of gram-negative bacteria may produce shock, a condition that unfortunately is often recognized late and is associated with a high mortality rate.

It appears likely that, in the patient, endotoxemia develops gradually probably over several hours. For this reason the common method of producing experimental endotoxemia in the dog by rapid injection of a lethal dose may not represent accurately the clinical situation in man.

The present study was undertaken to observe the effects of slow infusion of a lethal dose of endotoxin in the dog. For the purpose of comparison, a smaller group of dogs was given the same dose of endotoxin in the conventional manner—by a single rapid injection.

Endotoxin derived from gram-negative bacteria is believed to exert a sympathomimetic effect either directly or by sensitizing the animal to previously non-toxic levels of circulating catecholamines.[1, 2]

Through a microscope, Zweifach, Nagler and Thomas[3] studied vascular responses to endotoxin in the microcirculation in the rat mesoappendix *in vivo*. Topical application of epinephrine after a *sub-lethal* dose of endotoxin produced widespread vasoconstriction, with capillary-bed ischemia lasting several minutes. After a *lethal* dose of endotoxin, epinephrine reactivity exhibited a biphasic response. In the first hour, reactivity was increased, though less than after a sub-lethal dose; during the second, reactivity diminished; in the third, increased reactivity resulted in prolonged vasoconstriction and the terminal vessels remained unresponsive and dilated. Marked reactivity in the small veins led to the pooling of blood in the collecting venules.

Zweifach, Nagler and Thomas studied the effects of a slow infusion of endotoxin in the isolated, perfused rabbit ear. A *subthreshold* dose administered by this method produced prolonged, intense vasoconstriction.

Method

Of 19 healthy, adult, mongrel dogs in this study, 15 received endotoxin by slow infusion. The remaining four received endotoxin by rapid injection. Because the effects of rapid injection of endotoxin in the dog were already well studied in our laboratory, the latter group was kept small.

The endotoxin used in these experiments was lipopolysaccharide *E. coli* 0111:B4, prepared by the Difco Company of Detroit, Michigan, in a desiccated form and supplied in vials of 100 mg. All dogs received a dose of 5 mg./kg. body weight. In the slow infusion, this dose was added to 250 ml. of 5% dextrose in water and the infusion was administered over two hours via a P280 polyethylene cannula in the external jugular vein. For rapid injection the dose was administered in 5 ml. or less of sterile normal saline and given by the same route as the slow infusion.

All experiments were carried out under intravenous pentobarbital anesthesia, 30 mg./kg. body weight.

The blood pressure was monitored by a Statham transducer, linked with a Sanborn Poly-Viso recorder. Other parameters measured were the central venous pressure, hind-limb venous outflow, arterial pH, P_{CO_2}, HCO_3 and survival. The acid-base balance was studied using the Astrup method.

Results and Discussion

In a man with endotoxemia, blood pressure is said to decline gradually,[4, 5] while in the dog, the blood pressure falls precipitously after endotoxin injection, partially recovers to near-normal levels and finally declines.[2, 6]

---

*From the Surgical-Medical Research Institute and the University of Alberta Hospital, Edmonton, Alta.

†Supported by the Canadian Life Insurance Officers' Association Research Fellowship. Present address: Vernon Jubilee Hospital, Vernon, B.C.

‡Associate Professor of Surgery, University of Alberta Hospital, Edmonton.

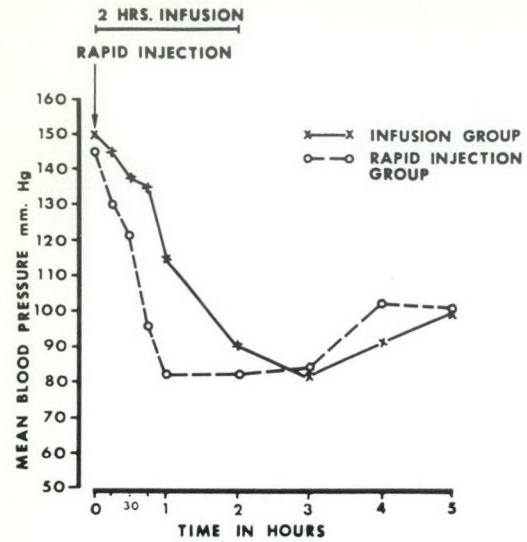

Fig. 1.—Changes in mean blood pressure after endotoxin administration. Note that, in the slow infusion group, the blood pressure gradually declines from the start of the infusion.

Because in man endotoxemia is not likely to develop suddenly as it does after the injection of a lethal dose of toxin in the experimental animal, the comparison may not be entirely valid. In this study, slow infusion of endotoxin in the dog produced a gradually developing endotoxemia and a general decline in mean blood pressure similar to that described in man. While the initial sudden drop is not seen, the decline in blood pressure at the end of two hours is identical with that produced by rapid

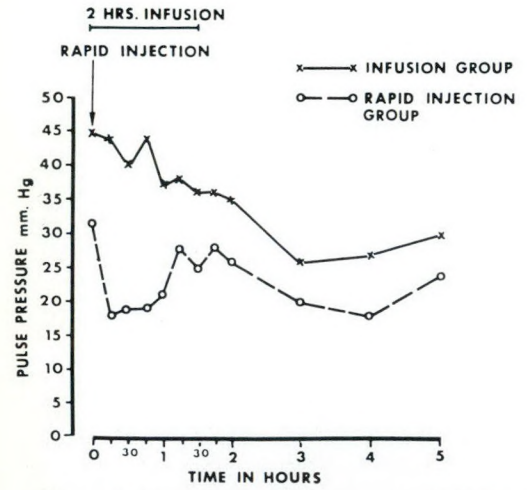

Fig. 2.—Changes in pulse pressure following endotoxin administration.

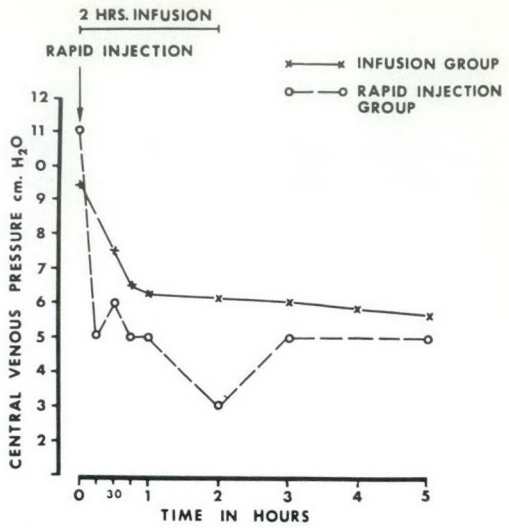

Fig. 3.—The effects of endotoxin administration on central venous pressure.

injection (Fig. 1). Further, there is a marked fall in the mean blood pressure during infusion at a time when only a fraction of the endotoxin has been administered.

During slow infusion the pulse pressure falls steadily—a trend that continues for a considerable period after the infusion has been discontinued. This contrasts with the response of the group receiving the rapid injection; in these dogs, after the initial drastic fall and subsequent fluctuations, the pulse pressure recovers to near-normal levels (Fig. 2).

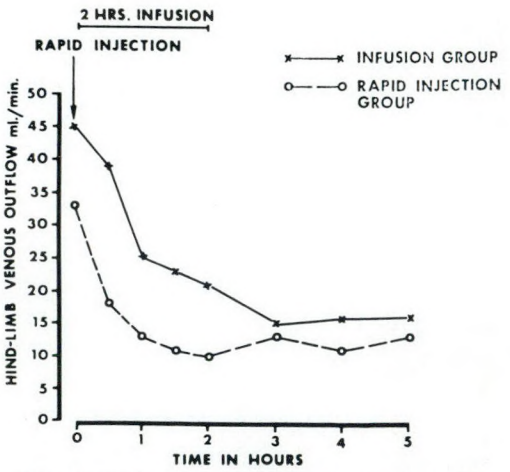

Fig. 4.—Reduction in hind-limb venous outflow due to endotoxin. Note the fall in the infusion group even at a time when only a fraction of the total dose has been administered.

In both groups the central venous pressure falls, but we observed no significant difference between them (Fig. 3). At one hour, when only one-half the endotoxin dose had been administered by slow infusion, the reduction in hind-limb venous outflow was equivalent to that produced by rapid injection of the full dose (Fig. 4).

The effects of endotoxin administration on the acid-base balance of the dog are shown in Figs. 5 to 7. Endotoxemia is accompanied by generalized vasoconstriction and reduced tissue perfusion. Increased lactic acid production lowers the pH of the arterial blood. The compensatory hyperventilation results in a fall in the P_{CO_2} (Fig. 6). At the same time, HCO_3 buffer is used up in an attempt to sustain the pH at normal levels (Fig. 7).

The effect on the arterial pH is illustrated in Fig. 5.

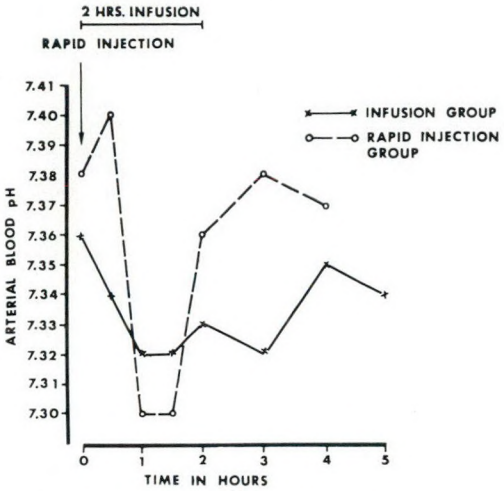

Fig. 5.—Changes in arterial pH following the administration of endotoxin.

Survival

Dogs surviving for one week were regarded as permanent survivors.

In the rapid injection group, two dogs survived, and the other two died at 19 and 39 hours respectively.

In the slow infusion group, five dogs survived. The other 10 died at intervals ranging from 6½ to 120 hours (6½, 14, 19, 19, 20, 37, 48, 72, 120 and 120 hours respectively).

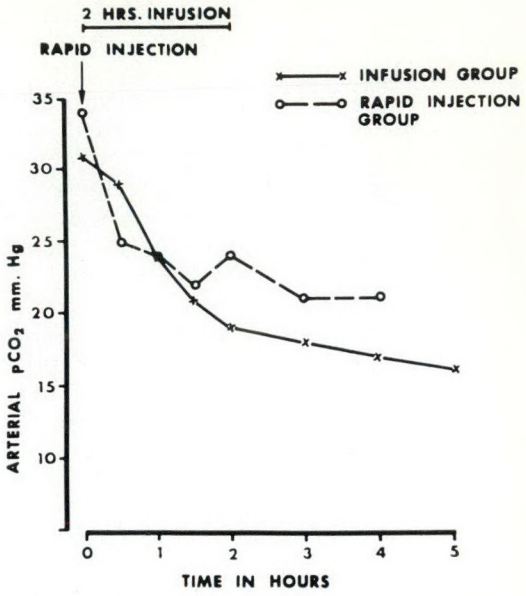

Fig. 6.—Fall in arterial P_{CO_2} due to hyperventilation which follows endotoxin administration. Note the progressive change from the start of the slow infusion.

Summary and Conclusions

Our results support the view that endotoxin derived from gram-negative bacteria

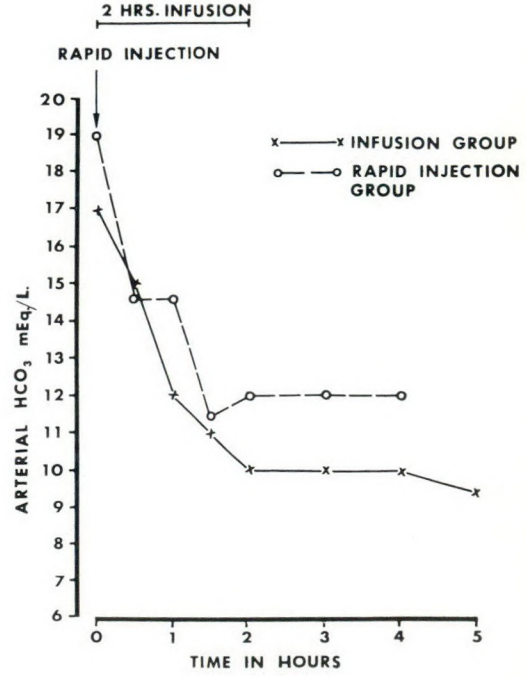

Fig. 7.—Arterial HCO_3 changes in endotoxemia. The HCO_3 is reduced from the start of the slow infusion.

produces significant hemodynamic effects in the experimental animal. The most significant observation in this study is the effect produced by slow infusion of endotoxin. Most parameters we studied had deteriorated even when only a fraction of the total dose had been administered. From the start this deterioration was progressive and comparable to, but more gradual than, that produced by rapid injection. Furthermore, the decline in the mean blood pressure showed the same gradual downward trend observed in endotoxin shock in man.

Because even relatively small doses of endotoxin appear to produce profound hemodynamic effects, endotoxemia must be recognized early in patients.

It is our impression from these studies that the slow infusion of endotoxin in the dog more accurately simulates clinical endotoxemia in man.

The technical assistance of Mr. Alexander Geczy is gratefully acknowledged.

References

1. Gourzis, J. T., Hollenberg, M. W. and Nickerson, M.: Involvement of adrenergic factors in the effects of bacterial endotoxin, *J. Exp. Med.*, **114:** 593, 1961.
2. Lillehei, R. C. and MacLean, L. D.: The intestinal factor in irreversible endotoxin shock, *Ann. Surg.*, **148:** 513, 1958.
3. Zweifach, B. W., Nagler, A. L. and Thomas, L.: Role of epinephrine in the reactions produced by the endotoxins of gram-negative bacteria. II. The changes produced by endotoxin in the vascular reactivity to epinephrine, in the rat mesoappendix and the isolated perfused rabbit ear, *J. Exp. Med.*, **104:** 881, 1956.
4. Rosenberg, J. C. *et al.*: Studies on hemorrhagic and endotoxin shock in relation to vasomotor changes and endogenous circulating epinephrine, norepinephrine and serotonin, *Ann. Surg.*, **154:** 611, 1961.
5. Vick, J. A., Lafave, J. W. and MacLean, L. D.: The effect of treatment of endotoxin shock on renal hemodynamics and survival, *Surgery*, **54:** 78, 1963.
6. Lillehei, R. C. and MacLean, L. D.: Physiological approach to successful treatment of endotoxin shock in the experimental animal, *A.M.A. Arch. Surg.*, **78:** 464, 1959.

Résumé

Comme il est probable que l'endotoxine s'accumule graduellement dans le sang du malade, les auteurs ont étudié les effets qu'exerce sur le chien une perfusion lente d'une dose létale d'endotoxine. Cette méthode d'administration tranche vivement avec la méthode courante de provoquer une endotoxémie expérimentale chez le chien, soit l'injection rapide d'une dose mortelle.

Sous anesthésie au pentobarbital, on a donné à 15 chiens, en perfusion lente, une dose mortelle d'endotoxine. Les auteurs ont enregistré et étudié la tension artérielle, le pouls, la pression veineuse centrale, le débit veineux de sortie des membres postérieurs, le pH artériel, la P_{CO_2}, et le HCO_3 et ils ont noté la survie.

L'endotoxine provenant de bactéries à gram-négatif provoque chez l'animal d'expérience des effets hémodynamiques considérables. Dès le début, la perfusion lente d'endotoxine a produit une détérioration progressive de la majorité des paramètres, altération qui est comparable, au point de vue quantitatif, à celle que provoque l'injection rapide mais qui survient plus graduellement. La tension artérielle moyenne a montré la même tendance décroissante qu'on observe chez l'homme souffrant de choc par endotoxine.

Les auteurs concluent que la perfusion lente d'endotoxine chez le chien reproduit avec plus de précision l'endotoxémie clinique chez l'homme.

THE CANADIAN JOURNAL OF SURGERY

All communications concerning this Journal should be marked "The Canadian Journal of Surgery" and addressed to the Editor, C.M.A. Publications, 129 Adelaide Street West, Toronto.

The Journal is published quarterly. Subscription is $10 per year ($5 per year for trainees in surgery), and starts with the January issue of each year. Single copies are $2.50 each, payable in advance. (It would be greatly appreciated if subscribers would please add bank exchange to their cheques.)

INSTRUCTIONS TO CONTRIBUTORS

Manuscripts

Manuscripts **in duplicate** of original articles, case reports, and other contributions should be forwarded with a covering letter requesting consideration for publication in *The Canadian Journal of Surgery*. Acceptance is subject to the understanding that they are submitted solely to this Journal, and will not be reprinted without the consent of the author and the publishers. Acceptance or rejection of contributions will be determined by the Editorial Board. As space is available, a limited number of case reports will be published. Articles should be typed on one side only of unruled paper, double-spaced, and with wide margins. The author should always retain a carbon copy of material submitted. Every article should contain a summary of the contents. The Concise Oxford Dictionary will be followed for spelling. Dorland's Illustrated Medical Dictionary will be followed for scientific terminology. The Editorial Board reserves the right to make the usual editorial changes in manuscripts, including such changes as are necessary to ensure correctness of grammar and spelling, clarification of obscurities or conformity with the style of *The Canadian Journal of Surgery*. In no case will major changes be made without prior consultation with the author. Authors will receive galley proofs of articles before publication, and are asked to confine alterations of such proofs to a minimum.

Reprints

Reprints may be ordered on a form which will be supplied with galley proofs. It is important to order these before publication of the article, otherwise an extra charge for additional type-setting will be made.

References

References should be referred to by numerals in the text. They should include in order: the author's name and initials in capitals, title of the article, abbreviated journal name, volume number, page number and year. The abbreviations of journal names should be those used by the National Library of Medicine, Washington, D.C., as published in *Index Medicus*. References to books should include in order: author's name and initials, title of book, number of edition (e.g. 2nd ed.), title of publishing house, city of publication, year of publication, page number if a specific reference.

Illustrations

A reasonable number of black-and-white illustrations will be reproduced free with the articles. Colour work can be published only at the author's expense. Photographs should be glossy prints, unmounted and untrimmed, preferably not larger than 10″ x 8″. Prints of radiographs are required and *not the originals*. The magnification of photomicrographs must always be given. Photographs must not be written on or typed on. An identifying legend may be attached to the back. Patients must not be recognizable in illustrations, unless the written consent of the subject for publication has been obtained. Graphs and diagrams should be drawn in India ink on suitable white paper. Lettering should be sufficiently large that after reduction to fit the size of the Journal page it can still be read. Legends to all illustrations should be typed separately from the text and submitted on a separate sheet of paper. Illustrations should not be rolled or folded.

Language

It should be clearly understood that contributors are at full liberty to submit articles in either English or French, as they please. Acceptance will be quite independent of the language of submission. If the contributor wishes, he may submit an informative summary of not more than 300 words in the language other than that in which he has submitted the article. For example, an article in English must carry an English summary and may, if the author wishes, carry a more detailed summary in French.

LE JOURNAL CANADIEN DE CHIRURGIE

Toute communication concernant le Journal devra porter la mention "Le journal canadien de chirurgie" et être adressée à l'Editeur, Publications de l'A.M.C., 129 Adelaide Street West, Toronto.

Le journal est publié trimestriellement. Le prix de l'abonnement est de $10. par an ($5. par an pour les médecins qui sont résidents en chirurgie) et commence avec le numéro de janvier de chaque année. Un exemplaire isolé coûte $2.50 et est payable d'avance. (Nous serions reconnaissants aux souscripteurs de vouloir bien ajouter à leur chèque le montant des frais bancaires éventuels).

INSTRUCTIONS A NOS COLLABORATEURS

Manuscrits

Les manuscrits d'articles originaux, de rapports cliniques etc. seront envoyés en deux exemplaires, accompagnés d'une lettre demandant qu'on veuille bien considérer leur publication dans ***Le journal canadien de chirurgie.*** Ils ne seront acceptés qu'à la condition qu'ils n'aient été soumis qu'à notre Journal et qu'ils ne soient pas réimprimés sans le consentement exprès de l'éditeur et l'auteur. L'acceptation ou le refus des articles soumis relève du Conseil de la publication. Si la place est disponible, un nombre limité d'histoires cliniques pourront être publiés. Les articles seront dactylographiés sur un seul côté d'un papier non ligné, à double espace et avec une large marge. L'auteur devra toujours conserver une copie au papier carbone du texte soumis. Tout article devra être accompagné d'un résumé. L'orthographe sera celle adoptée par le dictionnaire Larousse. Quant à la terminologie scientifique, elle sera basée sur le Dictionnaire des termes techniques de médecine ou tout autre ouvrage de référence sérieux. Le Conseil de la publication se réserve le droit d'apporter au texte les changements qu'il jugerait à propos pour assurer la correction grammaticale et l'orthographe, pour éliminer d'éventuelles obscurités ou pour rendre la présentation conforme au style du *Journal canadien de chirurgie.* Aucun changement important ne sera apporté au texte sans que l'auteur aît été préalablement consulté. Les auteurs recevront avant la publication des épreuves d'imprimerie de leur texte, auxquelles ils sont priés d'apporter le minimum de corrections.

Tirés-à-part

On pourra commander des tirés-à-part sur une formule qui est envoyée avec les épreuves. Il est important de les commander avant la publication de l'article, sous peine de devoir payer un supplément pour une nouvelle composition.

Bibliographie

Les références bibliographiques seront indiquées par des numéros dans le corps du texte. Elles comprendront dans l'ordre: le nom de l'auteur et ses initiales, en majuscules, le titre abrégé du Journal, le numéro du volume, le numéro de la page et l'année. Les abréviations admises pour les noms de revues sont celles qui figurent dans *l'Index Medicus* de la Bibliothèque Nationale de Médecine, Washington, D.C. Les renvois aux livres comprendront dans l'ordre: le nom de l'auteur, ses initiales, le titre de l'ouvrage, le numéro de l'édition (p. ex. 2ème éd.), le nom de la maison d'édition, la ville où elle est située et l'année de la publication; enfin, le numéro de la page s'il s'agit d'un renvoi précis.

Illustrations

Le journal accepte de publier gratuitement un nombre raisonnable d'illustrations en noir et blanc. Les reproductions de clichés en couleurs seront publiées aux frais de l'auteur. Les photographies seront imprimées sur papier brillant, ne seront ni montées ni calibrées et d'un format maximum de 8" x 10". En ce qui concerne les radiographies, nous demandons des copies et *non pas l'original.* On devra toujours fournir un agrandissement de microphotographies. Il ne faut jamais écrire ou dactylographier un texte quelconque sur les photographies. Une légende les identifiant pourra être jointe au dos. Dans les illustrations montrant des malades, ceux-ci ne pourront être reconnus, à moins qu'ils n'en aient donné le consentement écrit préalablement à la publication. Les graphiques et diagrammes seront dessinés à l'encre de Chine sur un bon papier à dessin blanc. Le lettrage devra être écrit en caractères assez grands pour que, après réduction proportionnelle au format du Journal, ils soient encore lisibles. Les légendes devant accompagner les illustrations seront dactylographiées sur une feuille indépendante du texte. Les illustrations ne seront ni roulées ni pliées.

Langue véhiculaire

Il doit être clairement établi que les collaborateurs ont pleine liberté de soumettre leurs articles en français ou en anglais, à leur choix. L'acceptation de l'article sera entièrement indépendante de la langue choisie par l'auteur. Si le collaborateur le désire, il peut décrire le contenu de l'article en un sommaire ne dépassant pas 300 mots et dans une langue différente de la langue choisie pour l'article lui-même. Par exemple, un article écrit en français doit comporter un résumé en français et peut, si l'auteur le désire, être accompagné d'un sommaire plus détaillé en anglais.

BOOK REVIEWS

AGING LIFE PROCESSES. Compiled and edited by Seymour Bakerman. 189 pp. Illust. Charles C Thomas, Publisher, Springfield, Ill.; The Ryerson Press, Toronto, 1969. $11.75.

In this monograph, one in the series of the Bannister Division of American Lectures on Living Chemistry, Dr. Bakerman and four collaborators view ageing processes in terms of biochemical changes. This publication is not a critical analysis of disease entities reflected in ageing but a well-integrated study of human biology in which the recent facts and theories on the underlying basis of the ageing processes are well documented and presented in an orderly fashion. The first chapter covers the many biological parameters used to describe ageing. In the following three chapters, the alterations with age of the informational macromolecules and of protein synthesis and metabolism are discussed. The age-associated changes in lipids and pigments are the subject of an important chapter and finally the many theories as to the cause of ageing are critically reviewed.

This monograph contains numerous bibliographical references and should prove to be well worth reading not only to human biologists, biochemists and pathologists but also to physicians who are turning more and more to chemistry in order to understand the underlying basis of life processes in health and disease.

CHIRURGIE PLASTIQUE CUTANEE DE LA MAIN CHEZ L'ENFANT ET L'ADULTE. R. Vilain and J. Michon. 158 pp. Illust. Masson et Cie, Paris, 1968. 59 F. $13.00 (approx.). Paperbound.

The monograph is a collection of the principles and techniques applied to surgery of the hand. The authors do not pretend to cover the wide field of surgery of the hand, but rather have selected certain topics of interest to them. The book contains a bibliography referring to various techniques for the procedures described by the authors. The other techniques are usually not commented upon.

Part of the text deals with basic rules governing surgery of the hand. The bulk of the text describes various well-known methods of replacing lost skin, of repairing finger and wrist injuries, and of certain aspects of finger amputation.

A few specific comments merit attention. Healing by second intention appears to be fairly common with the authors' cases. Medicated dressing to control wound granulation and scarring is suggested for moderately long periods before grafting. A "flag flap" as proposed by Levame, which is not frequently seen in American literature, may have some interesting applications for repair of small defects on adjacent fingers. A number of free skin grafts and pedicles are described for hand coverage.

Distally based, dorsal digital flaps are suggested for covering certain neighbouring defects of the fingers. Z-plasties and free grafts are described for the treatment of scar contractures of the palmar aspects of the joints.

It is interesting to note that the authors have a definite preference for general anesthesia, and that they almost never use local or regional anesthesia.

In general, this monograph is a collection of personal thoughts on certain aspects of hand surgery. It should be of interest to the hand surgeon because of the description of certain techniques not routinely used in hand surgery.

ADVANCES IN SURGERY. Vol. 3. Edited by Claude E. Welch. 403 pp. Illust. Year Book Medical Publishers, Inc., Chicago, 1968. $16.50.

The latest volume of this series includes chapters of sufficient length to be definitive on the following subjects: selective splanchnic angiography; the preservation of intact organs; non-specific ulcerative colitis; management of war wounds; and pathophysiology, diagnosis and management of pulmonary embolism. There is a great deal that is new and important to the surgeon on each of these topics. The present format permits a longer and more complete presentation than would be possible even in a review article in most journals. The illustrations are excellent and the bibliographies are exhaustive.

These subjects, presented by experts, justify the concept that timely topics presented in depth in one volume can be a most useful reference text. This series, and this volume in particular, is recommended to general surgeons and house officers in surgery.

CHRISTOPHER'S TEXTBOOK OF SURGERY. 9th ed. Edited by Loyal Davis. 1493 pp. Illust. W. B. Saunders Company, Philadelphia; W. B. Saunders Company Canada Limited, Toronto, 1968. $23.25.

The changes made in this book since the previous edition in 1964 have enhanced its value as a general reference textbook in surgery. New chapters have been added on the following subjects: oncology, diseases of degeneration, congenital diseases, trauma, artificial organs and transplantation. Despite these additions the length of the book has only increased by 26 pages. This appears to have been accomplished by reducing the discussion of more highly specialized fields, such as open heart surgery. Also, the chapter on physical medicine and rehabilitation has been extensively rewritten and shortened to bring it

more in line with a textbook of general surgery. The same approach has been used in the chapter on the heart and great vessels. At the same time changes have been made to update the chapter regarding changing techniques and methods. The chapter on congenital diseases is short but again principles of treatment have been stressed and lengthy discussions on fine details are avoided. The result of this approach has been to make this a better textbook of general surgery. An adequate bibliography is provided throughout for those who seek finer details.

The new chapter on diseases of degeneration takes into consideration the increasing numbers of old people seen in a general surgical practice. It is both interesting and a worthwhile addition to the book. The principles of treatment are outlined in some detail in the chapter on trauma. For completeness this is certainly an essential addition to the book.

Little change has been made in the chapters on the stomach and duodenum, and small and large bowel. The portion on the liver and biliary system has been rewritten by a new author and has been updated regarding the use of hepatic arteriography, isotope studies and scanning. There has been little change in the chapter dealing with the genitourinary system, although portions have been rewritten. Adequate coverage is provided in orthopedics for the general surgeon. The new chapter on artificial organs provides information regarding cardiopulmonary bypass, renal dialysis and prosthetic heart valves.

A good summary regarding problems, results, techniques and future possibilities is provided in the new chapter on transplantation of tissues and organs by T. E. Starzl and L. Brettschneider.

Generally speaking, this standard and well-established textbook in general surgery has been updated and improved.

DISEASES OF THE NOSE, THROAT AND EAR. 11th ed. John Jacob Ballenger. 948 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1969. $35.75.

This textbook is too detailed for the medical student. Many of its chapters would be ideal in a textbook or reference book for residents or practising otolaryngologists, but many other chapters require updating, especially those that refer to current therapy.

The descriptions of clinical anatomy and physiology of sinuses and nose are adequate. However, the section on embryology makes little reference to the formation of the palate and mouth.

The chapter on inflammatory diseases of the nose and sinuses covers recent advances in virology and Dr. Montgomery has modernized the surgical treatment of sinus infections. The chapters on complications of sinus disease and tumours of nose and sinuses are comprehensive for residents or otolaryngologists. This book also contains sections on the salivary gland and the temporomandibular joint, subjects which are barely mentioned in most textbooks.

The classification of the chronic granulomas of the ear, nose and throat will aid the practising otolaryngologist. However, the pathological descriptions are not detailed enough for the resident. Similarly, the sections on tumours of the nasopharynx and salivary glands should be given in more detail, especially the classification and pathology.

The coverage of the larynx is excellent. The sections on laryngeal trauma and acute laryngeal inflammations contain recent advances in management and treatment. The chapter on laryngeal carcinoma contains the recent classification and treatment of the disease and makes special reference to conservative surgery in laryngeal carcinoma.

The discussion of the anatomy and embryology of the ear given here is too detailed for the medical student but the section on the physiology of hearing has been modernized by an account of Von Bekesy's theory. The chapter on acute inflammatory diseases of the middle ear contains very little about serous otitis media and "glue" ears which are so prevalent now. The chapter on otosclerosis contains a good historical and pathological description of this disease and mentions recent surgical methods in treating it.

As is appropriate, the chapter on industrial noise exposure and hearing loss is more detailed than in previous textbooks.

In summary, this textbook is too detailed for the medical student, yet not sufficiently comprehensive for the otolaryngology resident. It would, however, be a good reference book for the practising physician or otolaryngologist.

FUNDAMENTAL TECHNIQUES OF PLASTIC SURGERY AND THEIR SURGICAL APPLICATIONS. Ian A. McGregor. 298 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1968. $5.60.

Mr. McGregor has again, in the fourth edition of his book, maintained the same stringent guidelines he set out in his first edition—brevity and clarity. In this era of expanding medical texts and increasing costs, the author has resisted the real temptation of enlarging the size of the book with a subsequent increase in price. One is treated to the basic principles in plastic and reconstructive surgery with no frills attached. The text is concise and the drawings are simple and easily understood. In this new edition, the author has explained in more detail the multiple Z-plasty, and the principles involved, and has

deleted the section involving miscellaneous conditions in general surgery. This comprehensive text is to be strongly recommended to any surgeon involved in ablative or reconstructive surgery, or the surgery of trauma.

CHRONIC ULCERATIVE COLITIS. A Lifelong Study. J. Arnold Bargen. 123 pp. Illust. Charles C Thomas, Publisher, Springfield, Ill.; The Ryerson Press, Toronto, 1969. $9.00.

Dr. J. Arnold Bargen probably has seen more patients with ulcerative colitis than any other physician. A record of his experience, therefore, is invaluable. All physicians called upon to treat ulcerative colitis should read this book and in particular the chapters devoted to the clinical description of the disease, its diagnosis and its complications.

Although this reviewer, a surgeon, may be looked upon with suspicion because of his specialty, he is on solid statistical ground when he opposes Bargen's views on the prognosis of children with ulcerative colitis. Devroede and Sauer recently reviewed the Mayo Clinic experience with children suffering from ulcerative colitis and studied the records of 396 patients who had been followed up to 43 years. In his book (page 15), Bargen says that, with proper care, one-half of the children will recover from their disease; yet Devroede and Sauer found that 20% died every 10 years. There was no decrease in mortality rate with time and only 27% lived to be 57 years old. Bargen also says that the suggestion of prophylactic proctocolectomy for young patients is arbitrary and untenable. Although he recognizes that children run an increased risk of carcinoma, he makes the common mistake of saying that 40 out of 401 patients developed the malignancy, therefore suggesting a 10% incidence. This relation of a number increasing with time (the number of cancers) to a number decreasing with time (the number of patients) is bound to give a conservative estimate and is fraught with error. Devroede and Sauer, using actuarial methods, found a 20% risk each 10 years after the first decade: after 43 years, 69% had developed a cancer of the large intestine! Not only "inexperienced" (page 95) physicians consider the prognosis of such cancers hopeless, the Mayo Clinic workers duplicated Brooke's earlier data, finding that 50% of their group who developed malignancy died within six months; the five-year survival was only 18%!

These new figures might well disillusion the observer about the ability to achieve major success with a medical treatment. Ulcerative colitis is notoriously unpredictable and, with the exception of salicylazosulfapyridine (Azulfidine), no treatment has been studied in a randomized controlled fashion. An elemental diet can be given to these patients with good results, but when Devroede and Sauer move up from this artificial regimen to food, they encounter all the difficulties pointed out by Kramer when he studied ileostomy output. Should the foundation diet be low in residue or in crude fibres' content? What is a low-residue diet? Should milk be restricted only in the 10% of patients with ulcerative colitis who have a disaccharidase deficiency? The disillusionment with medical treatment deepens when one notes that the Mayo Clinic study found a similar survival rate between 1919 and 1953, and between 1953 and 1966. On the other hand, Devroede and Sauer did find a better ($P<.05$) survival in patients submitted to proctocolectomy than in unoperated patients. Theirs was a retrospective study and obviously patients doing well were not operated upon. Many readers will regret that, in his résumé, Dr. Bargen does not even mention operative treatment.

However, despite this important reservation about the validity of Bargen's views on prognosis, this book can be recommended to any physician who has patients with ulcerative colitis in his care.

FRACTURES OF THE FACIAL SKELETON. 2nd ed. N. L. Rowe and H. C. Killey. 896 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1968. $33.50.

The two senior authors have once again published an outstanding text with the added assistance of seven new contributors. Four chapters have been added to this edition, namely, care of the unconscious patient, use of drugs in maxillo-facial surgery, maxillo-facial technology and a very unusual section on the medical-legal aspects in the treatment of maxillo-facial injuries.

There is an increase in the number of photographs, drawings and radiographs. These are presented in a more compact and comprehensive fashion due to the increase in page area. This permits a step-by-step presentation which cannot be excelled and the organizational format has been changed to augment this method of delivery. The only possible criticism that could be directed towards this new edition is the failure to incorporate the expanded historical background into the introductory chapter.

This book is a necessary addition to the library of every trauma surgeon of dental or medical orientation. Few texts are presented with such authenticity!

INHALATION THERAPY PROCEDURE MANUAL. Thomas J. DeKornfeld and Don E. Gilbert. 114 pp. Charles C Thomas, Publisher, Springfield, Ill.; The Ryerson Press, Toronto, 1968. $8.00.

This manual, written especially for the University of Michigan Medical Center, shows step-by-step inhalation therapy procedures and techniques. The step-by-step instructions are extremely detailed but apply only to the types and makes of equipment available at

that particular medical centre and are therefore limited in their general application.

The chapter on nebulizers (aerosol generators) should more clearly differentiate between small-volume nebulizers used for giving medication and large-volume nebulizers used for humidification.

A short section outlines, in summary form taken from the manufacturer's literature, the characteristics of some of the drugs used in inhalation therapy.

The job descriptions apply to the classification of therapists and technicians as given by the American Association for Inhalation Therapy and the American Registry for Inhalation Therapists. They do not uniformly correspond to the classification used by the Canadian Society of Inhalation Therapy Technicians but are certainly of interest.

Overall, the manual is useful and adaptable to the requirements of other hospitals as a guide for the establishment of procedure manuals for Inhalation Therapy Departments.

LESIONS TRAUMATIQUES DES TENDONS DE LA MAIN. J. Michon and R. Vilain. 107 pp. Illust. Masson et Cie, Paris, 1968. 39 F. $8.60 (approx.). Paperbound.

This publication contains, in the first part, the views presented by the authors at a congress held in 1961. The second section contains comments on lesions of the flexor and extensor tendons. The monograph consists of a selective compilation of pathophysiology of the hand and of tendon surgery.

Prosthetics tendon-sheet studies are reported. In some of their extensively undermined cases, the authors use suction drainage. Rehabilitation by physiotherapy following a tendon repair is said to be started around the thirtieth day for flexor as well as for extensor tendons; in certain cases, however, postoperative immobilization of extensor tendons varies from three to six weeks according to whether there is a simple transection or whether there is loss of substance.

The authors describe various treatments of mallet-finger deformity, button-hole deformity and extensor ruptures.

Verdan's method of zoning the hand is used by the authors in dealing with flexor-tendon surgery. They recommend primary suturing of tendons in all areas of the hand before the age of 20. They feel that such primary suturing is occasionally indicated between the ages of 20 and 45, while it is to be rarely done in patients over 45.

Some points of technique used more commonly in the French-speaking community are described. This may be of particular interest to the hand surgeon.

This review is of interest to people already familiar with the pitfalls of hand surgery. As mentioned earlier, it presents personal views on selected problems of hand surgery.

METABOLIC RESPONSE OF THE BURNED ORGANISM. Rajko Dolecek. Edited by Wiktor W. Nowinski. 233 pp. Illust. Charles C Thomas, Publisher, Springfield, Ill.; The Ryerson Press, Toronto, 1969. $12.25.

This book, first published in Prague in 1964, has been revised and brought up to date for the first English edition. The first chapter reviews the physiology of metabolism and energy release and discusses the reaction of the endocrine glands to the burn. The reaction of the adrenal glands is discussed in detail; paragraphs on anabolic hormones, antidiuretic hormones and the thyroid glands are included. The metabolic response of the burned organism is discussed in the light of biochemical and morphological changes. The last chapter is devoted to therapeutic implications.

Burns research has followed different directions in different centres. In many respects, the approach outlined in this book appears strange to us—for instance the following statements, "The state of the nervous system is very important for many adaptive reactions of the burned organism", "A cellular level of adaptation" and "Simple procedures can save lives and eliminate the pain of thousands." The author considers that the concept of stress and adaptation is important and the name of Selye is mentioned frequently. Therapeutically the authors have had good experimental and clinical results with a neuroplegic mixture called the M_2 mixture. It is of interest that no reference is made to the work of Laborit and some others who have been active in this field.

MICROLARYNGOSCOPY AND ENDOLARYNGEAL MICROSURGERY. Techniques and Typical Cases. O. Kleinsasser. Translated by Paul W. Hoffman. 128 pp. Illust. W. B. Saunders Company, Philadelphia; W. B. Saunders Company Canada Limited, Toronto, 1968. $13.50.

The application of microscopic techniques to endolaryngeal surgery represented an important advance in surgery of the larynx. The appearance of this book is timely and reflects the experience of the author in more than 600 microlaryngoscopies in a three-year period.

The early part of the book reviews instruments and technique and will be a valuable guide to the surgeon embarking on this type of work. This is followed by a short account of relevant photographic techniques which, if followed, will prevent a great deal of unnecessary experiment. The bulk of the book is taken up by a detailed analysis of the author's case material. It is profusely illustrated and the beauty of the work lies in the 100 coloured photographs of the appearance of the larynx in health and disease. These, surely, are unequalled anywhere in the litera-

ture and on their own make the volume worth studying.

Many line sketches indicate specific endolaryngeal surgical techniques. It is a pleasure to see endolaryngeal surgery advance from crude biopsy to carefully delineated incision and excision.

Some of the surgical techniques described, however, are unorthodox when judged by standard North American practice. For instance, endolaryngeal excision of a vocal cord carcinoma would have few followers, and endolaryngeal arytenoidectomy and submucosal hemicordectomy for bilateral vocal cord paralysis are hardly orthodox therapy.

These minor criticisms should not detract from the book which has been well translated in an easy style. It deserves to be widely studied and will find a place in the library of anyone interested in diseases of the larynx.

NOUVEAU TRAITE DE TECHNIQUE CHIRURGICALE. Tome XII. Fasc. 1. Foie et voies biliaires intra-hépatiques. René Bourgeon et Marcel Guntz. 324 pp. Illust. Masson et Cie, Paris, 1968. 120 F. $26.50 (approx.).

Le "Nouveau traité de technique chirurgicale" sous la direction des professeurs Jean Patel et Lucien Léger est une entreprise formidable de haute valeur scientifique. Plusieurs tomes ont déjà été publiés et ceux que nous avons pu examiner ne nous ont certes pas déçus.

C'est avant tout un ouvrage de technique chirurgicale mais où on retrouve les éléments essentiels d'anatomie et la description des techniques d'exploration. Dans tous les volumes, l'iconographie est abondante et claire et d'une grande précision anatomique.

Le tome XII ne diffère en rien des autres volumes quant à la qualité du matériel et la valeur des présentations. Dans ce premier fascicule du tome XII on traite du foie et des voies biliaires intra-hépatiques. Les premiers chapitres sont consacrés à l'anatomie chirurgicale et aux procédés d'examens nécessitant quelques manœuvres chirurgicales.

Le deuxième chapitre traite des affections chirurgicales du foie proprement dit et, ce qui est d'un intérêt particulier pour nous, c'est la section sur les traumatismes et les techniques de réparation des lésions hépatiques.

La section sur les résections hépatiques dites "réglées" est excessivement bien présentée et très utile pour tout chirurgien intéressé à la chirurgie abdominale. C'est une revue importante de toutes les meilleures techniques décrites dans la littérature médicale française.

L'illustration des techniques de transplantation hépatique est très bien faite et peut être très utile aussi en chirurgie expérimentale.

Le dernier chapitre traite de la chirurgie des voies biliaires intra-hépatiques, ici encore, chaque technique est bien décrite et les illustrations complètent la clarté du texte.

En résumé, ce tome XII possède les qualités d'excellences de ses prédécesseurs et ne peut manquer d'être d'une grande utilité à tous les chirurgiens intéressés à la chirurgie digestive.

PLANNING OF SURGICAL CENTERS. Basic Studies. Ervin Pütsep. 122 pp. Illust. Lloyd-Luke (Medical Books) Ltd., London; Natur och Kultur, Stockholm, 1969. 80/-. $10.00 (approx.). Paperbound.

At one time or another, most physicians and surgeons become involved in the planning of patient facilities. Few, however, are experts in this field and all too frequently errors, which should have been detected earlier, are recognized only when the building is completed. The brief outline of planning presented in this book, therefore, is most welcome. The first paragraphs discuss aspects of postoperative wound infection and show how an appropriate building can minimize wound infections. The chapter on spatial requirements starts with the following sentence: "Of the errors which became evident during this study, poor space planning in shape of underdimensioned rooms is one of the most prominent." Space requirements for various functions are described in detail for staff, surgical theatres, radiology, laboratories, postoperative units, facilities for housekeeping and stores. The author devotes special attention to surfaces and openings (floors, walls, ceilings, doors, windows), and environmental specifications such as lighting, colour, acoustics and air conditioning. Technical specifications related to water supply, electrical installation and medical gases are discussed in the last chapter. Although short, this book appears to be complete and has a surprisingly exhaustive bibliography. This book should be of value to those involved in the planning of major hospital facilities, but also to those involved in comparatively minor projects in their own practice.

NERVES AND NERVE INJURIES. Sydney Sunderland. 1161 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1968. $39.75.

Dr. Sunderland has been Professor of Anatomy at the University of Melbourne for many years and this volume is the culmination of his life-long interest in peripheral neurology. It is a monumental work for one author to have produced and runs to over 1000 pages of double-column text.

The eight parts are: (1) Anatomical and Physiological Features of Peripheral Nerve Fibres and Nerve Trunks. (2) Degeneration. Regeneration. A Classification of Nerve Injury. (3) Clinicopathological Considerations. (4) Bones, Joints, Muscles and Motor Function. (5) Peripheral Sensory Mechanisms. (6) Peripheral Sympathetic Mechanisms. (7) Diagnosis and Treatment. (8) Individual Nerves.

While the bibliography, in keeping with the high standard of scholarship, appears to be complete, there are few references to the literature after 1964, which, in these days of rapid discovery, means that the book is not completely up-to-date even at the time of publication. For example, there is no consideration of the revelations of the electron microscope, and recent work will not be found on the nature and formation of myelin or the biochemistry of axoplasm. In a large textbook written by one author, this is inevitable. But if this is recognized as an authoritative and full text on peripheral nerves up to about 1964, the reader will not be disappointed. It is excellently planned and produced and qualifies as one of the most important works on the subject in the English language.

POSTOPERATIVE FRUHKOMPLIKATIONEN. Grundlagen der Krankenbehandlung auf der Wachstation. Kurt Wiemers, Ernst Kern, Maria Günther and Hilmar Burchardi. 248 pp. Illust. Intercontinental Medical Book Corp., New York; Georg Thieme Verlag, Stuttgart, West Germany, 1969. DM 49,00. $13.30 (approx.).

Written by a team of surgeons and anesthesiologists, this book will be of particular value to physicians and surgeons responsible for postoperative care in smaller centres. This general approach justifies the first chapter which covers the pathophysiology of respiration, coagulation, fluid and electrolyte balance and other systems that are important in the postoperative phase. The various complications that follow a surgical operation are then discussed individually and, finally, the various treatment procedures are discussed in some detail.

REPAIR OF HERNIAS. A Handbook of Operative Surgery. Mark M. Ravitch. 189 pp. Illust. Year Book Medical Publishers, Inc., Chicago, 1969. $11.00.

This book gives a wide coverage of all the hernias encountered in the abdominal wall, and also deals with diaphragmatic hernias. It not only demonstrates technique, but also the physical examination of inguinal hernias at the groin and the indications for operation. For groin hernia repairs, the author advocates local anesthesia and demonstrates its use. A large series of well-drawn illustrations shows each maneuver and the various techniques recommended. The author demonstrates the classical Halsted-Ferguson type of operation without displacement of the cord, as distinct from the more common Bassini repair. There is a good chapter on the management of the sac in sliding hernia. A chapter is devoted to the subject of ventral hernias. The author is in favour of the use of pneumoperitoneum to prepare the abdomen to receive the contents of the large ventral hernias. Whether this is a valid recommendation could be argued. He is in favour of the use of fascia lata and does not favour the use of prosthetic materials. One extensive chapter is devoted to omphalocele and this is well described. The repair of diaphragmatic hernias is also quite well described although some of the older methods of repair, such as the Allison's repair, seem to be stressed somewhat unduly.

On the whole, this is a useful book for anyone who wants the detailed technique of hernia repair. It represents one man's view on the subject, and not all readers will necessarily agree with the recommendations. However, the clarity of the text and the illustrations make it worthwhile reading.

TRAITEMENT CHIRURGICAL DE L'APLASIE VAGINALE. La rectocolpoplastie par la technique de J. Soustelle et H. Villiers. J. Soustelle, H. Villiers et P. Vuillard. 103 pp. Illust. Simep Editions, Lyon, France, 1967. Price not stated. Paperbound.

Les auteurs nous présentent une technique chirurgicale comme traitement de l'aplasie vaginale qui a plusieurs avantages et très peu de désavantages en ce qui concerne les résultats.

Les auteurs décrivent d'abord la morphologie pathologique telle que rencontrée dans les cas de l'aplasie vaginale avec les variations d'anomalies congénitales qui l'accompagnent. Ils procèdent ensuite à une description assez détaillée de l'anatomie normale des organes voisinants et surtout de la vascularisation du côlon sigmoïde, du rectum et de l'anus avec toutes les variations qu'on peut trouver.

Ayant décrit les anomalies et l'anatomie anormale et normale, les auteurs nous présentent ensuite un compte rendu de l'évolution des techniques employées jusqu'ici pour corriger cette anomalie en décrivant dans chaque cas les avantages et désavantages.

La rectocolpoplastie que les auteurs décrivent après ceci a pour but de conserver les avantages acquis dans les opérations déja développées, soit la sécurité de la dissection rectale par voie coccygienne, l'exploration abdominale et la facilité de mobilisation sigmoïdienne et la mobilisation rectale réduite au minimum qui, par ce fait, permet de conserver une vascularisation rectale intacte. Ajoutée à ces avantages, la technique décrite assure aussi la continence sphincterienne absolue par la conservation totale du canal anal. La description de leur technique n'est pas trop détaillée, mais présente les points importants qui sont nécessaires pour atteindre les avantages déja mentionnés.

Le livre est bien écrit, facile à suivre et les idées sont bien développées. L'impression rend la lecture facile et les illustrations, quoique pas trop nombreuses, sont simples et adéquates.

(Continued on page 507)

(Continued from page 504)

Nous croyons que ce volume est une contribution de valeur qui nous présente une technique très interessante, mais on doit dire que le chirurgien qui voudrait entreprendre cette opération, après avoir lu ce bouquin, ne pourrait le faire à moins d'avoir beaucoup d'expérience dans la chirurgie sigmoïdienne et rectale.

ULCERATIVE COLITIS. J. C. Goligher, F. T. de Dombal, J. McK. Watts and G. Watkinson. 365 pp. Illust. Baillière, Tindall & Cassell Ltd., London; The Macmillan Company of Canada Limited, Toronto, 1968. $13.75.

This book gives an excellent review of the entire subject of ulcerative colitis. The bibliography is extensive and the ideas of other authorities are frequently presented. The portion devoted to pathology is contributed by B. C. Morson of St. Mark's Hospital, London. It is clearly presented and a comparison is drawn between the pathology of ulcerative colitis and granulomatous colitis.

The chapter pertaining to clinical and radiological features is particularly lucid. The great number of radiological signs associated with this disease are carefully analyzed and their relative values assessed. Clinical correlations with radiological findings are drawn, and an attempt is made to show the prognostic values of various signs.

The authors discuss the natural history of the disease and the influence that medical and surgical treatments have had. Generally the book is surgically oriented and the surgical techniques are described together with the surgical complications and their management. A practical discussion of the minutia of ileostomy management is a useful addition.

The book consolidates the modern thinking regarding the etiology, diagnosis, management and complications of the disease. All physicians and surgeons interested in this disease will find the book valuable and refreshing reading.

SURGERY OF THE CHEST. 2nd ed. Edited by John H. Gibbon, Jr., David C. Sabiston, Jr. and Frank C. Spencer. 954 pp. Illust. W. B. Saunders Company, Philadelphia; W. B. Saunders Company Canada Limited, Toronto, 1969. $35.10.

This superb book on the surgery of the chest covers the subject in all its aspects. The second edition is a considerable expansion on the first edition of six years ago. There are now 42 chapters supplied by 51 different authors. The editorship of John Gibbon has been expanded to three by the addition of Sabiston and Spencer. The chief reason for the expansion lies in the 13 chapters which deal with the surgical treatment of diseases of the heart and great vessels. In all, there are 27 new chapters. It is impossible to single out any one chapter for comment. This reviewer is particularly interested in the chapter on the mediastinum by Sabiston and Oldham. This valuable review contains an interesting, large, accumulated list of statistics on the types of lesions encountered in the mediastinum. Congenital lesions of the lungs and emphysema is another chapter that is well handled. Something more might have been devoted to mediastinoscopy. There is just one brief paragraph on this subject on page 451. The chapter on the suppurative and fungal diseases of the lungs is excellent and the demonstrations of the surgical technique of lobectomy are also good.

The whole book is well produced. The text is clear and readable, and the illustrations throughout are of a high order. This is the type of book that should be in every surgical library as a reference for both undergraduate and graduate students, and it will find its place on the shelves of every surgeon interested in either thoracic or cardiac surgery.

PRACTICAL UROLOGY. Chester C. Winter. 249 pp. Illust. The C. V. Mosby Company, St. Louis, 1969. $12.10.

This volume is an outline of urology with emphasis on recent advances. The book deviates from the usual order of subject matter. Instead of each chapter dealing with a single uropathy and its impact on the various urological structures, each chapter deals with a single organ but includes all uropathies pertaining to that organ. Modern concepts in urological investigation are described or discussed, such as arteriography, antegrade pyelography, radioisotope methodology, etc. For the uninitiated, the introductory chapter contains a glossary defining a number of urological terms used in the text. Of particular interest is the chapter on the kidney in which various aspects of renal physiology and pathology are dealt with including a section on renal transplantation. The chapter on the ureter deals with such important entities as retroperitoneal fibrosis, vesicoureteral reflux and ureteral diversion. A chapter on the adrenal gland clearly describes clinicopathological entities and diagnostic methods. At the conclusion of each chapter the author asks a number of questions which emphasize important points developed within the chapter. Following the questions there is a list of recommended readings both current and classic and, finally, there is a list of available motion pictures. Illustrations, both photographic and drawings, are of good quality and well selected. This book is obviously too short to be in any respect exhaustive, nevertheless it contains a wealth of information and gives a lucid and authoritative account of many of the current concepts in urology.

(Continued on page 509)

in place of morphine or Demerol, reach for

(Continued from page 507)

SURGERY FOR CEREBROVASCULAR INSUFFICIENCY (STROKE). With Special Emphasis on Carotid Endarterectomy. Jesse E. Thompson. 96 pp. Illust. Charles C Thomas, Publisher, Springfield, Ill.; The Ryerson Press, Toronto, 1968. $11.50.

This is an excellent review and discussion of the problem of cerebrovascular occlusive disease and the surgery thereof. It is a well-arranged book with excellent indexing. The author's clinical material and personal experience are probably the largest in the world. He makes no attempt to oversell the various surgical procedures, although in one or two areas the implication is a bit ambiguous. For instance, when discussing results of carotid endarterectomy, Dr. Thompson mentions 372 patients in whom **blood flow was** *restored* by operation in all instances, yet he is talking about partially occluded carotids. Later he states that an increase in cerebral blood flow by surgical means with relief of ischemia *may* thus result in the reversal of neurological deficits previously considered irreversible.

The reproduction of radiographs is excellent. The book is liberally illustrated and has the even greater merit of being short. One might conceivably raise the question as to the indications for a book such as this in such a rapidly changing field, but the techniques and principles which the author has given are not likely to change even though timing, indications and early diagnosis may all improve.

WASSER- UND ELEKTROLYT-FIBEL. Diagnostik und Therapie des Flüssigkeitshaushaltes. 2nd ed. Bruno Truniger. 161 pp. Illust. Intercontinental Medical Book Corp., New York; Georg Thieme Verlag, Stuttgart, West Germany, 1969. DM 16,80. $4.50 (approx.). Paperbound.

This small compendium of diagnosis and therapy of water and electrolyte balance does not pretend to cover completely the theoretical knowledge in this area. This book was written for the practitioner treating electrolyte imbalances in his daily practice. In the introduction the author admits that he may have oversimplified the situation in certain areas. The necessity for a second edition only two years after the first shows that this general approach is justified. The author describes briefly the physiological and pathophysiological basis for the treatment of water and electrolyte imbalances. In the second part, he describes the diagnostic procedures including history, physical examination and laboratory tests. In the chapter on therapy, the various therapeutic procedures are outlined emphasizing the use of electrolyte concentrates which are added to glucose-in-water solutions. In the last chapter, special problems are discussed such as the postoperative period, burns, shock and diabetes.

Books Received

Books are acknowledged as received, but in some cases reviews will also be made in later issues.

Abdominal Operations. Vols. 1 and 2. 5th ed. Rodney Maingot. 1827 pp. and index. Illust. Appleton-Century-Crofts, Educational Division, Meredith Corporation, New York, 1969. $45.50.

Achalasia of the Esophagus. F. Henry Ellis, Jr. and Arthur M. Olsen. Vol. 9 in the series Major Problems in Clinical Surgery. 221 pp. Illust. W. B. Saunders Company, Philadelphia; W. B. Saunders Company Canada Limited, Toronto, 1969. $9.75.

Atlas of Gastrointestinal Surgery. Komei Nakayama. 649 pp. Illust. J. B. Lippincott Company, Philadelphia; J. B. Lippincott Company of Canada Ltd., Toronto, 1968. $46.00.

Basic Surgical Physiology. Edited by Frederick W. Preston and John M. Beal. 508 pp. Illust. Year Book Medical Publishers, Inc., Chicago, 1969. $27.50.

Cardiovascular Surgery 1968. Council on Cardiovascular Surgery, American Heart Association, Scientific Sessions, Bal Harbour, Miami Beach, Florida, November 21-24, 1968. American Heart Association Monograph Number 24. Edited by C. Frederick Kittle. 274 pp. Illust. The American Heart Association, Inc., New York, 1969. $4.00 (U.S. funds). Paperbound.

Chronic Ulcerative Colitis. A Lifelong Study. J. Arnold Bargen, 123 pp. Illust. Charles C Thomas, Publisher, Springfield, Ill.; The Ryerson Press, Toronto, 1969. $9.00.

La Ciné-Angiographie Sélective des Artères Coronaires. G. Lavaurs and F. Rijtano. 114 pp. Illust. L'Expansion Scientifique Française, Paris, 1968. 22 F. $4.80 (approx.). Paperbound.

Controversy in Obstetrics and Gynecology. Edited by Duncan E. Reid and T. C. Barton. 414 pp. Illust. W. B. Saunders Company, Philadelphia; W. B. Saunders Company Canada Limited, Toronto, 1969. $16.75.

Diseases of the Nose, Throat and Ear. 11th ed. John Jacob Ballenger. 948 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1969. $37.75.

Dynamic Factors in Diagnosis of Supratentorial Brain Tumors by Cerebral Angiography. Norman E. Leeds and Juan M. Taveras. 122 pp. Illust. W. B. Saunders Company, Philadelphia; W. B. Saunders Company Canada Limited, Toronto, 1969. $16.20.

Edward Stevens. Gastric Physiologist, Physician and American Statesman. Edited by Stacey B. Day. 179 pp. Cultural and Educational Productions, Cincinnati and Montreal, 1969. Price not stated.

Harvey Cushing. Selected Papers on Neurosurgery. Edited by Donald D. Matson, William J. German and a Committee of the American Association of Neurological Surgeons. 669 pp. Illust. Yale University Press, New Haven and London; McGill University Press, Montreal, 1969. $19.25.

Illustrated Handbook in Local Anaesthesia. Edited by Ejnar Eriksson. 160 pp. Illust. Year Book Medical Publishers, Inc., Chicago, 1969. $14.25.

The Liver. Colston Paper No. 19. Edited by A. E. Read. 405 pp. Illust. Butterworth & Co. (Publishers) Ltd., London; Butterworth & Co. (Canada) Ltd., Toronto. 1967. $31.50.

La Main Rhumatoïde. The Rheumatoid Hand (in French and English). Under the direction of Raoul Tubiana. 269 pp. Illust. Expansion Scientifique Française, Paris, 1969. Price not stated. Paperbound.

Narkose. Eine Einführung. Ludwig Stocker. 257 pp. Illust. Intercontinental Medical Book Corp., New York; Georg Thieme Verlag, Stuttgart, West Germany, 1969. DM 9,00. $2.45 (approx.). Paperbound.

Non-Insulin Producing Tumors of the Pancreas. Modern Aspects on Zollinger-Ellison-Syndrome and Gastrin. International Symposium at Erlangen, July 16th and 17th, 1968. Edited by Ludwig Demling and Rudolf Ottenjann. 213 pp. Illust. Intercontinental Medical Book Corp., New York; Georg Thieme Verlag, Stuttgart, West Germany, 1969. DM 29,00. $7.90 (approx.). Paperbound.

Practical Urology. Chester C. Winter. 249 pp. Illust. The C. V. Mosby Company, St. Louis, 1969. $12.10.